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An Address.[1]

MEDICAL CARE IN THE WELFARE STATE.

By H. HASTINGS WILLIS,

President, New South Wales Branch of the British Medical Association.

I THANK my colleagues of the Council for the honour bestowed on the public medical officers of New South Wales by my election as President of this Branch of the British Medical Association for the year 1955.

I am not the first public medical officer to occupy that post. A glance at the photographs which adorn the far wall of this hall will show that several public medical officers have occupied that place before me. In my time I remember Dr. A. A. Palmer and Dr. R. J. Millard, two worthy servants of the New South Wales Government, who were Presidents of the Branch in 1918 and in 1926 respectively, and I understand there were others before them. But they earned the favour of their colleagues by personal merit. I am well aware that my presence on the Council is entirely due to my having been chosen by my colleagues in the public services as their spokesman in medico-political affairs during the last quarter of a century. I am glad to know that my election is regarded by my friends as a compliment to them, and I trust it will result in improved relations between them and their colleagues in competitive private practice.

I understand that between 20% and 25% of members of this Branch of the Association occupy salaried positions—quite a respectable minority, which is not represented on our Branch Council in proportion to its numerical strength and is not represented on our Federal Council at all. I understand there is a similar state of affairs in Victoria.

Not all salaried members of this Branch are in Government employ—I estimate that half of them are—and unfortunately not all public medical officers are members of this Branch—an additional reason why relations between public and private practitioners should be good.

Thirty-six years ago Professor F. P. Sandes, in his presidential address for the year 1919, drew the attention of his hearers to the growing strength and efficiency of the public medical services. His remarks were not uncomplimentary, but they seemed to me to be actuated by apprehension rather than admiration. He seemed to fear alleged potentialities for harming private practitioners, and I think he correctly reflected the opinion of the leaders of the profession in that age. But what harm have public medical

[1] Read at the annual meeting of the New South Wales Branch of the British Medical Association on March 31, 1955.

officers done to their fellow members during the years which have passed since Professor Sandes sounded his alarm? None whatever, either here or in England.

I trust you will agree with me that friendly understanding, not fear, should characterize the relations between all the various sects into which our profession has become divided. Public medical officers desire friendly relations with private practitioners, and seek reciprocity.

It is clear that the profession will have much to do with public servants in the future. Business men spend much time and often money in cultivating good relations with those with whom they do business. I do not suggest that public servants should be "cultivated" in this way, for they would resent it, but I do suggest the wisdom of appreciating the peculiar position of public servants in a democratic community. They are servants of the Crown and, like all servants, are expected to be faithful to their employer, and this legal and moral obligation is reinforced by the religious sanction of an oath of allegiance and a declaration of secrecy. They are deprived of many freedoms and cannot be expected to be over-careful of the freedoms of others. In fact, freedom is not a bureaucratic concept. Public servants strive for regularity and efficiency which at times is incompatible with freedom. In the course of his official duties a public servant may not have an opinion of his own; he must correctly reflect in his daily work the opinions and policy of the Government of the day and must change his attitudes with every change of Government—a feat which at times calls for no small degree of mental agility and adaptability. I find that my colleagues have difficulty in understanding the impersonality and anonymity of the public servant; yet a little thought will show that things must be as they are. To allow public servants a personal opinion and a personal discretion in the performance of their duties would be dangerous. If public servants ever come to have a personal discretion in the performance of their public duties, on that day, and not till then—despite some irresponsible statements to the contrary—will the public service govern the country.

Here I ask your indulgence for a recruiting appeal. Though the number of salaried medical officers is appreciable and is slowly increasing, there is room for more.

Our Federal Council has adopted a policy of medical control of medical activities, but this cannot be implemented unless more young doctors choose a career of medical administration. Conditions in the services are not as good as they ought to be, but much has been done by the British Medical Association, in conjunction with other bodies, for which public medical officers are duly grateful. Further improvements are to be expected, and it may be that in the near future here, as behind the iron curtain, medical organization and administration will be regarded as a medical specialty and will be graded and paid for accordingly. In the meantime, we need far more men of administrative ability and sound medical knowledge. Such men, if willing to endure petty annoyances and frustrations, and to give attention to tedious detail, will find in the various Government and semi-Governmental organizations a satisfying opportunity of serving their generation while earning an honest though modest living.

It is the duty of the President-Elect to give an Occasional Address at this annual meeting of the Branch. Fortunately it may not be a policy speech, as some in other Branches would have it be, for as a representative of a minority group I am particularly unfitted to formulate a policy for the Branch; nor may it be a pronouncement on behalf of the Council, for the new Council has not yet met. Custom ordains that it should not be a technical address, but should deal with some subject of general interest to all members of the Branch. As medical politics have been uppermost in all our thoughts in recent years, I propose to offer for your consideration some comments on new features of medical practice, under the title "Medical Care in the Welfare State". I shall direct my remarks to the younger members of the Branch, as I think that in all our medico-political discussions we should concern ourselves chiefly with the interests of our younger members, for the future is theirs. We should be orientated to the future rather than mindful of the past. We should seek to secure conditions which will continue to attract men of ability and high character to the medical profession and allow them to give of their best in the service of their fellow men.

The political concept of a Welfare State is not new. It is customary to regard it as an aftermath of the second World War, but it is centuries old. The social legislation of recent years, which appears revolutionary to us, is merely a recent acceleration of social evolution which has been in progress since the days of King George III. It is customary to regard Lord Beveridge as the founder of the Welfare State in England, and Mr. Benjamin Chifley as its founder here, and with some reason. But Lord Beveridge, for his part, has disclaimed any credit or blame. He maintains that the Welfare State of England was founded by Mr. Winston Churchill, Mr. Lloyd George and Mr. Herbert Samuel, who won a parliamentary election in England for their political party in 1906 by an advanced programme of social reforms. However, these had been advocated for many years by others.

George III was, I think, the first ruler who recognized any obligation to ensure the welfare of his subjects. Before him, rulers—when they recognized any obligation to their subjects at all—were content to protect them against external foes and maintain law and order at home so that they might earn their living in safety; but King George III, at his accession in 1760, declared that he would promote the happiness and prosperity of his people. That the King's ideas were not ahead of his times is shown by the passage through the House of Commons in 1772 of a bill providing for the payment of old age pensions. This bill failed to pass the House of Lords, and it was really the destruction of the political power of the House of Lords in the second decade of this century which made possible that social legislation which has so profoundly altered the pattern of medical practice in Great Britain in recent years.

I remind you that it was George III who sent the First Fleet to these shores, so it may be said that New South Wales has always been a Welfare State. Certainly, "*salus populi suprema lex*" has been the guiding principle in much of our legislation since the institution of responsible government in 1855. It is usual to ascribe to the late Senator John Cash Neild the credit of inaugurating social benefits for the needy in this State. At a parliamentary election in 1895 he won the seat of Paddington by advocating old age pensions. After election he continued his agitation by securing the appointment of a Parliamentary Select Committee and of a Royal Commission of Inquiry, and by the other customary methods of political propaganda. So successful was he that within ten years old age pensions were paid throughout the Commonwealth —first in New South Wales in 1900, and within a few years of federation by the Federal Government throughout Australia. Since then all political parties have not been slow to follow Mr. Neild's example, and have offered the electors more and bigger benefits. The practice has not ceased yet, since political leaders have warned the profession that there are more benefits to come. Clearly the Welfare State is not yet fully developed in Australia.

The social legislation of recent years may be defended as a practical application of that spirit of kindliness—that *caritas* which Saint Paul commended to the Corinthians along with faith and hope, and declared to be the greatest of these three. Whether our parliamentarians were inspired by the teachings of the Apostle, or actuated by a desire to strengthen the nation politically and economically by a more equal distribution of wealth or to ensure to the less wealthy a share of the prosperity which came to us after the second World War (as was Mr. Chifley's avowed object), or whether they were moved by the less worthy motive of pleasing the electorate by gifts, the effect of their legislation has been to take from those that have much, according to their ability to pay, and to give to those that have little, according to their needs.

High taxation and benefits are characteristics of a Welfare State. That high taxation should produce adequate revenue, a high state of production is necessary, and this is dependent on the efficiency of men and machines. As

the efficiency of men is dependent in part on their health, the medical profession is expected to aid production by caring for the workers' health. This is primarily the duty of those of our colleagues who practise industrial medicine, or as they prefer to call it, occupational medicine. But when they fail, as they often will from causes outside their control, it becomes the duty of those who practise curative medicine to ensure the return of the worker to his post as early as possible. The duty of the doctor to his patient in the Welfare State is different from what it was in ages past. In the Victorian age the doctor was satisfied to save life and ease pain. With the growth of medical knowledge he has essayed to cure disease, and with some success. Now he is required to do all that and more. He is now to remove his patient's disability and restore him to his place as a happy earning member of the community. Disability rather than disease will interest the doctor of the future—or rather he will be interested in disease only as a cause of disability, interpreting disability not only as connoting impairment of earning capacity, but also as a threat to life, or interference with the comfort and enjoyment of life. The care of the patient in the Welfare State will be a matter of management rather than of treatment.

Not only in maintaining high production, but also in the distribution of benefits, is the help of the medical practitioner needed.

Even though medical tests of eligibility for benefits may be applied—as our Association desires they should be—by doctors specially employed for that purpose, whose income may not be influenced by the displeasure of disappointed applicants, certificates and reports in increasing numbers will be required from private practitioners. This may be distasteful, but it is unavoidable. In the Welfare State doctors are clerks, and it would be wise to give students to understand, at the commencement of their course of training, that they are going to be clerks when they qualify. Good legible handwriting will be as great an asset as a good bedside manner.

A fountain pen is the first tool of trade that a medical student acquires. He uses it for making notes, and he would do well to continue to use it for that purpose until the end of his career. The keeping of notes, which at present is done badly or not at all, will be a major responsibility of the doctor of the future if he is to serve his patients faithfully in the Welfare State. Nevertheless, the principal function of the doctor will be the management of disability.

During the greater part of my life I have been concerned with disability rather than disease, but I do not propose to offer advice as to how patients should be managed; for I have dealt with residual disability after doctors had done their best—with failures rather than successes in management. I find it easier, therefore, to find fault than to suggest remedies, and I realize that destructive criticism is of value only as a spur to positive effort. However, I trust you will permit me to refer to two results of faulty management which I think deserve the serious attention of the profession. I refer to doctor-made disabilities, and to the addictions. The amount of iatrogenic disability in the community is not creditable to us. It usually is a neurosis, and like all neuroses occurs in susceptible patients —those of defective personality. To detect defective personality is not easy for the doctor who sees a patient for the first time in his consulting room; the family doctor acquainted with the patient's home environment and medical history can do better.

We are all familiar with the neurotic embroidery with which some patients, notably claimants for compensation, influenced largely by a subconscious motive of gain acting far too often on a plane very close to consciousness, embellish a real organic disability. Such patients should be given a hopeful prognosis, and be advised to return to work as soon as possible. Hope is a more valuable medicament in these cases than all the drugs in the pharmacopœia and the most expensive proprietary products; while to be induced by the patient to give frequent certificates of unfitness is to be induced to do him a real disservice.

Apart from neurotic embroidery, there are neuroses which arise from faulty diagnosis, unnecessarily grave prognosis or unwise management.

When in doubt many doctors assume the worst and treat the patient accordingly. This may conserve the doctor's reputation, but it does not serve the patient's interests. I submit that the patient, not the doctor, should be given the benefit of the doubt, and, when the diagnosis lies between organic disease and functional disorder, the condition should be treated as neurotic. I cannot remember an instance in thirty years' experience in which a patient with organic disease has come to harm through being treated as neurotic, but there have been many instances of aggravation of neurosis by an unwarranted diagnosis of serious organic disease.

In patients with symptoms suggestive of chronic nervous disease, or referable to the heart, we must be particularly on guard. Many chronic nervous diseases appear to be neuroses in their early stages, but as their prognosis is hopeless and their treatment futile, nothing is lost, but much gained, by improving the mental state of the patient.

Cardiac neurosis causes much distress to patients and their friends, and often causes serious impairment of earning capacity. We should take care not to cultivate it, or fix it, by undue concern about minor cardiac symptoms. Much false invalidism was caused during the first World War by the heart-conscious doctors of that period who fixed neurotic symptoms on the heart, just as the stomach-conscious doctors of the second World War have left us a legacy of functional dyspepsia and similar psychosomatic disorders.

We must be watchful for somatic manifestations of mental disorder and avoid cultivating them. *"Primum non nocere"* is good advice in diagnosis and prognosis as well as in treatment. More harm is done by bad prognosis than by bad treatment. Moreover, we should not soothe our uneasy consciences by thinking that a diagnosis—say of coronary sclerosis or myocardial degeneration—will prove correct in time. Certainly most people will develop organic heart disease if they live long enough; but anticipatory diagnosis of that sort is not creditable.

As for the addictions, some are vices and call for police action, even though they occur in the mentally weak. I am old-fashioned enough to refuse to regard vice and crime as medical or social diseases. By all means let the doctors cure these addicts, or try to do so—as the lawyers think they can—but in the disciplinary atmosphere of a penal establishment rather than as honourable patients in a palatial medical institution. Of a truly medical character, however, are those addictions which arise out of legitimate medical treatment of grave physical illness or neurosis —usually the latter. Psychiatrists warn us that treatment of these addictions is difficult; they stress the importance of prevention. These addictions arise insidiously, often over a period of years, and an unwary doctor may discover too late that he has been pandering to an addiction. The number of fatal and near-fatal cases of barbiturate poisoning which we see suggests that addiction to these drugs is much too common. Doctors need to be on guard to prevent it.

An unusual addiction which has caused me much concern is addiction to oxygen. Unfortunately, patients so affected are gravely ill or think they are, hence attempts to wean them are resented by the patients and their friends. The more necessary, therefore, is prevention. Fortunately, oxygen is not on the Government's free list, and its cost is a deterrent to private patients; but when the cost is not burdensome or when it is met by a third party, a troublesome and costly addiction may develop, which is difficult to terminate.

For the proper management of the disabled, a knowledge of home conditions is necessary, and I note with satisfaction that the Welfare State is driving the doctor into the homes of his patients.

Colleagues whose opinions I respect tell me that whereas ten years ago two patients were examined in consulting rooms to every one examined at home, the proportion is now three to four, and this proportion is likely to diminish if the fee for a medical service is the same whether given at home or at the doctor's rooms.

I see many advantages in home treatment, which I think is the special province of the general practitioner. He should jealously preserve it. For the understanding of neuroses, which form so large a part of general practice, a knowledge of the patient's domestic relationships and home environment is essential, and such knowledge is also advantageous in dealing with psychosomatic and somatic disorders. How often is a patient cured by a holiday or by removal to hospital, only to relapse on returning home? In such cases, clearly, alteration of the home environment is the essential part of management, or, failing that, instruction of the patient in ways of adjusting himself to his environment. Removal to hospital will, of course, be necessary in many instances, but we should get away from the notion that a hospital is the proper place for every patient who is seriously ill. Better is it for the patient, and the State, that he be treated at home, with the assistance of the diagnostic facilities of an out-patient clinic and the services of visiting nurses and domestic aids.

In this connexion, I draw your attention to the psychiatric service of the Municipality of Amsterdam, whose physicians do not examine patients at consulting rooms, but only in the patients' own homes. These physicians find admissions to hospital seldom necessary. I commend this to you as a pattern of general medical practice in the future.

No address would be appropriate to this occasion that did not make some reference to the cost of medical care, for this matter is of much political importance at the present time. We have in Australia the best scheme of national health service yet devised. It is envied by the medical professions of other lands. But this scheme is seriously threatened by its high cost. I know that some practitioners are impatient of any mention of costs. They think their sole concern is the welfare of the patient. Should doctors count the cost? Had I answered that question forty years ago I should have said "No". I should have reflected the opinion of my teachers, as do most young doctors in the first decade after their graduation. Such an attitude was not inappropriate to those times. The cost of drugs was then small, hospital accommodation was adequate and within the reach of those who needed it, and the doctor-patient relationship was a simple one, the patient employing and paying the doctor, and therefore from self-interest being economical of the doctor's services.

Social evolution has proceeded far in two generations. Drugs are now much more efficient than those of old, but extraordinarily costly; hospital accommodation is provided with great difficulty and at high cost; and, most important change of all, a third party has intruded into the doctor-patient relationship, and this third party pays the greater part of the cost. Relieved of most of his financial responsibility, the patient is no longer economical, and his pressure on the doctor results in extravagance with drugs and medical attention. This change of patient pressure on the doctor is in my opinion the main cause of the great and increasing cost of medical care, rather than any moral deterioration of the profession, as our enemies suggest. In my opinion we should count the cost, and in all cases consider whether the benefit of the treatment we prescribe for the patient is commensurate with the cost to the third party who pays, whether the third party is the patient's employer, an insurance company or the Welfare State. We should recognize the interest of the third party in our medical care, but place strict limits upon it. He should not be allowed to question the quality of the service to the patient—the patient will demand, as he has the right to demand, the best possible treatment. His doctor will be proud to give it, and will be wise if he ensures that it is given at the least possible cost.

In conclusion I ask for a realistic approach to the medico-political problems which confront us. We live now in a Welfare State which has not yet reached full development. Many social benefits have been given in this generation, and we have been warned that there are more to come.

We must adapt our attitudes and customs to the changing circumstances of the times. We know that those organisms and institutions which adapt themselves survive, while those that cannot, or will not, go under in the battle of life. The medical profession will not go under; it will adapt itself, as it has in the past, possibly reluctantly, but nevertheless satisfactorily; and our patients, who are really our friends, and whom we should continue to regard as our friends, will make it easy for us to adapt ourselves, for they have need of our services. Now, as at the dawn of history, the mass of the people will "honour a physician for the need that they have of him", and will consider a medical practitioner to be "worth many men when the job to be done is pulling out arrows".

TRIETHYLENE MELAMINE (TEM) IN THE TREATMENT OF MALIGNANT LYMPHOID DISEASE.

By C. K. HAMELY AND T. I. ROBERTSON.

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RAPID advances are now occurring in the chemotherapy of the malignant diseases of hæmatopoietic tissue. As basic structural formulæ become established it is inevitable that many more substances will be developed. With each drug careful trial eventually determines its correct place in therapy and its relationship to established effective agents. The present paper reports our conclusions about the use of triethylene melamine (TEM), one of the most recently developed of these drugs, and is based on our experience with 41 patients over a period of eighteen months.

HISTORICAL BACKGROUND.

The use of TEM in malignant disease was suggested by a series of investigations starting with the discovery of mustard gas over ninety years ago. In 1860 Guthrie and Niemann first synthesized *bis*(2-chloroethyl) sulphide and noted that it was vesicant and damaging to the eyes. In 1917 at Ypres, when it was used by the Germans as a military weapon, the most obvious effects were again on the skin, eyes and respiratory tract. However, in a fragmentary fashion, it became evident that other tissues, including the hæmatopoietic system, were also sensitive. By 1939 the systemic effects in animals had been accurately tabulated but were largely ignored. In 1935 Ward first prepared a nitrogen mustard, *tris*(2-chloroethyl) amine. With the advent of World War II the whole subject was thoroughly investigated from the military aspect. The therapeutic potential also became better understood, and its action in malignant lymphoid disease has since been reported widely. Oral administration of this drug was prevented by severe gastro-intestinal symptoms. In 1948, Haddow, Kon and Ross prepared substances which had groupings characteristic of the nitrogen mustards, the most efficient against rat carcinoma being R48 (N.N-di(2-chloroethyl)-β-naphthylamine). The implication of a satisfactory tumour-inhibitory substance suitable for oral use suggested clinical trial in malignant lymphoid disease. Fair results were obtained (Matthews, 1950; Gardikas and Wilkinson, 1951; Galton, 1951), especially in leuchæmia, but R48 did not represent a great advance in treatment. The search for substances with nitrogen-mustard-like formulæ suitable for oral administration led to experiments with triethylene melamine, a compound used in Germany in the rayon industry (Evans, 1949). In America, Lewis and Crossley (1950) and Burchenal *et alii* (1950) noted inhibition of mouse sarcoma and leuchæmia. At the same time in England, Rose, Hendry and Walpole (1950) found considerable inhibition of growth in rat carcinoma and, encouraged by this, administered the drug to human patients. Extensive

clinical trials followed. Paterson and Boland (1951) reported the intravenous use of the drug. Karnofsky *et alii* (1951), having used the drug in a large series of patients, competently defined many of the indications and limitations of its intravenous and oral use in a wide assortment of malignant diseases. Amplification and fresh opinions have since been provided by Rundles and Barton (1952), by Gellhorn, Kligerman and Jaffe (1952), by Silverberg and Damashek (1952), by Kravitz, Diamond and Craver (1952), by Meyer *et alii* (1952), and by others. The subject has recently been reviewed by Axelrod, Berman and Murphy (1953).

Chemical Properties.

TEM is a white crystalline powder structurally related to nitrogen mustard and especially to the active ethyleneimonium transformation product formed from nitrogen mustard in tissue fluids. Figure I (from Karnofsky *et*

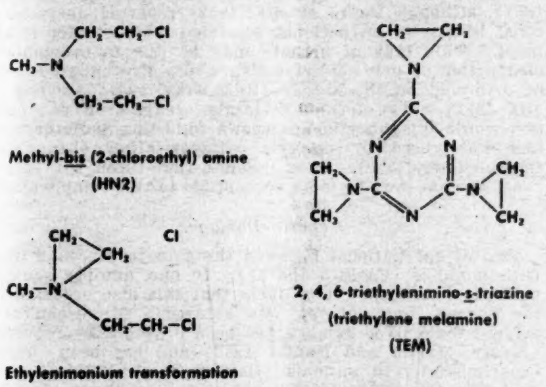

Figure I.

Showing the chemical relationship between nitrogen mustard and TEM. (From Karnofsky *et alii*, *A. M. A. Arch. Int. Med.*, April, 1951.)

alii, 1951) shows the chemical formulæ of these three substances. TEM is stable in alkaline solutions, but in acid medium the unstable, biologically active ethyleneimonium cation is formed with an extreme avidity for organic molecules. Gellhorn and Kligerman (1952) state that exhibition of the drug in the fasting state and alkalinization of the gastric juice should prevent this reactive form combining with substances in the gut and thus allow absorption of the whole dose. Our experience substantiates this. When absorbed, the reactive form of the drug combines with many cell proteins and enzyme systems and inhibits and destroys the function of susceptible cells. Goldacre, Loveless and Ross (1949), and again Loveless and Revell (1949) have suggested that the specific action of this type of substance depends on its combination with contiguous chromosome fibres in a cross-linking system, causing fragmentation and destruction of the chromosomes. This power is connected with the ability to pass into cyclic ethylene-imonium forms. The cell is most susceptible immediately prior to mitosis, when the chromosomes have reduplicated to produce a system of parallel identical fibres; therefore rapidly growing cells are most sensitive. These chromosome changes have been quantitatively evaluated by Hendry *et alii* (1951) in tumour tissue and bone marrow from treated rats.

The Present Investigation.

We have given TEM to 37 patients, selected for treatment with this drug because of generalised disease of hæmatopoietic or lymphoid tissue or because of resistance to radiotherapy. There were 12 patients with Hodgkin's disease, 10 with chronic lymphocytic leuchæmia, nine with lymphosarcoma, three with follicular lymphoma, and three with reticulosarcoma. The diagnosis was confirmed in each case by biopsy of a lymph gland. In addition we gave the drug to one patient with *polycythæmia vera*, to two with malignant melanoma and to one with Löffler's syndrome, making a total of 41 patients in all. Post-mortem examinations were made on 11 of the 20 patients who died whilst under treatment.

The investigation commenced at a time when extreme variations in dosage were being reported. Therefore it seemed useless to calculate dosage on a body-weight basis, and we have prescribed the drug in multiples and fractions of five milligrammes. The initial dose has varied from 2·5 to 15 milligrammes, no more than five milligrammes being given in any one day. In the case of the larger doses, five milligrammes were given on successive days. The drug was exhibited orally, in a standard way. A teaspoonful of bicarbonate of soda dissolved in a glass of water was given on waking, followed half an hour later by the dose. No food was eaten for a minimum of two hours. All patients were advised to stay in bed or rest for the whole day.

The first few patients were treated as in-patients until we became more familiar with the drug, but subsequently all except the very ill were treated as out-patients. The hæmoglobin value and the numbers of leucocytes and platelets were estimated before treatment and the bone marrow was occasionally examined. Renal function tests were performed on some of the later patients. After the first dose of TEM the patients were examined at weekly intervals, the result of the peripheral blood count of that day being available. When the numbers of granulocytes and platelets had stopped falling, the interval between visits was extended, depending on the success of the remission.

We define remission as the period of benefit derived in relation to the patient's well-being and capacity for work when accompanied by objective improvement, and consider it terminated by return of symptoms, enlarging gland masses or pathological rise in the number of leucocytes, even though further treatment is not necessarily given.

In the following sections we present our own findings about this drug in regard to its general effects on the hæmatopoietic system, its toxic effects and lastly its efficacy in the treatment of the different types of malignant lymphoid disease.

Hæmatological Effects of TEM.

Effect on Granulocytes.

One of the cells most sensitive to TEM is the neutrophile cell. Reduction in number begins within a few days of an oral dose and continues for two to four weeks and then gradually returns to pre-treatment levels (Figure II). In our series all grades of depression occurred, including extreme neutropenia with recovery in one patient (Case 21), and fatal agranulocytosis as part of a pancytopenia in two others (Cases 3 and 11). In these last two cases the neutrophile cell count continued falling after the expected recovery time (Figure III). We have encountered three cases of eosinophilia. In two, pronounced eosinophilia was caused by TEM (Figure IV), a phenomenon which has been reported previously (Paterson and Boland, 1951). In the other, a case of Hodgkin's disease, a high eosinophile cell count present before treatment was reduced in parallel with the neutrophile cell count (Case 9).

Effect on Lymphocytes.

Mature normal lymphocytes are susceptible cells, but have good powers of recovery. From the point of view of management their behaviour is not important. The malignant cell of lymphosarcoma and chronic lymphocytic leuchæmia is especially sensitive. In these diseases the lymphocyte count commences to fall quickly, and sometimes continues to fall for as long as ten weeks (Figure V) before gradually returning towards former levels.

Effect on Platelets.

The platelets are as sensitive as the neutrophile cells (Figure II). The maximum fall occurs usually within

three weeks, but reduction in numbers sometimes continues for as long as six weeks. Recovery to pre-treatment level is the rule, but in some of our cases the count has remained at a permanently lower level, a change difficult to attribute entirely to TEM in these progressive diseases. Thrombocytopenia, causing transient purpura, occurred in three of our cases (Cases 5, 19 and 34), and was part of a fatal pancytopenia in three others (Cases 3, 11 and 22).

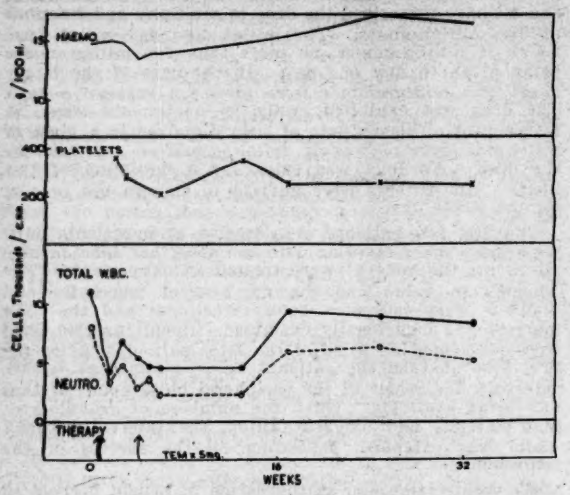

FIGURE II.

Case 32. Graph showing fall and subsequent recovery of the neutrophile cells and later rise in hæmoglobin value with TEM treatment.

Effect on Hæmoglobin Value.

In malignant lymphoid disease the hæmoglobin value falls under TEM therapy only when there is serious marrow depression. In the average successfully managed case its level shows only minor fluctuations. On several occasions we have seen it rise after treatment, with improvement in the patient's general condition (Figure II). In *polycythæmia vera*, the erythrocytes being more sensitive than normal, the red cell count and hæmoglobin value usually decline gradually over some months after an initial large dose.

Effect on the Marrow.

We have not studied the marrow systematically in our cases. From other workers it is clear that the reduction in the number of cells in the peripheral blood is due to marrow depression (Karnofsky *et alii*, 1951; Kravitz, Diamond and Craver, 1952). The most severe effects occur in patients with advanced disease and a previously damaged marrow. Granulopoiesis and thrombopoiesis are affected first, and erythropoiesis only when damage is severe. There is nothing to be gained by routine myelography, and predictions about dosage, response and toxicity can best be made by a clinical assessment of each patient and study of the peripheral blood.

TOXIC EFFECTS.

Minor Effects.

About one-quarter of our patients had no side effects at all. The majority complained of lethargy. Gastro-intestinal symptoms—nausea, vomiting and diarrhœa—occurred in at least 50%, usually on the day of administration only. Skin rashes also occurred, and we noted urticaria twice, and two instances of a generalized punctate erythema. These all responded quickly to simple treatment. Euphoria occurred in one patient, and was quite as pronounced as in classical disseminated sclerosis.

Major Effects.

Hæmatopoietic Effects.

We have shown that leucopenia, granulocytopenia and thrombocytopenia are readily produced. This depression of the bone marrow is the most dangerous toxic effect.

Renal Toxicity.

Two of our patients (Cases 20 and 31) died of uræmia, in our opinion precipitated by TEM; one was suffering from chronic lymphocytic leuchæmia and the other from lymphosarcoma. In both these diseases there occur rapid destruction of large amounts of malignant lymphoid tissue and release of large quantities of uric acid. This complication has been encountered by other authors (Wright *et alii*, 1952; Bayrd *et alii*, 1952; Karnofsky *et alii*, 1951; Kravitz, Diamond and Craver, 1951). To date there is no certain evidence that TEM has a direct nephrotoxic action in therapeutic doses (Karnofsky, 1951; Axelrod *et alii*, 1951), although Bayrd *et alii* (1952) reported unspecified renal lesions in all patients who died whilst under treatment. This type of uræmia may be due to mechanical obstruction by uric acid crystals, or to a direct toxic action of uric acid on the kidney (Karnofsky, 1954; Axelrod *et alii*, 1951). The former certainly occurred in one case of chronic lymphocytic leuchæmia following radiotherapy and was cured by ureteric catheterization (Lear and Oppenheimer, 1950). It is possible that those with prior renal damage may be more susceptible to this complication.

Hepatic Damage.

Two of our patients followed the same course and died with jaundice (Cases 3 and 11). In one, autopsy showed toxic liver damage. It is likely that this also occurred in the second, but autopsy was refused. Microscopically evident toxic liver damage has been occasionally reported (Beizer, Makler and Hanno, 1952) and has been caused experimentally in animals (Hendry *et alii*, 1951).

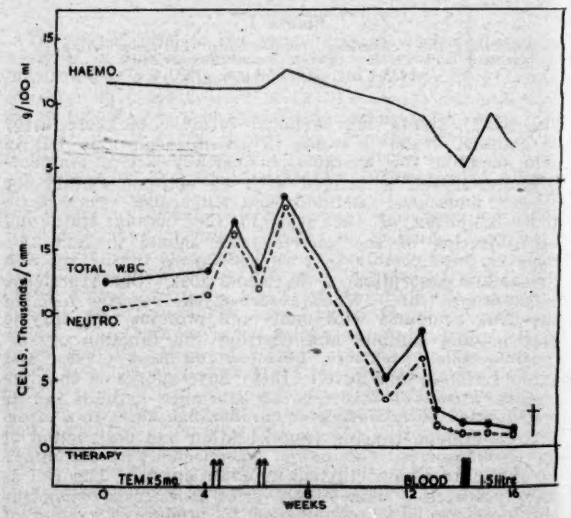

FIGURE III.

Case 11. Graph showing agranulocytosis produced by TEM.

Gastro-Intestinal Effects.

We have been impressed by severe, profuse, watery, almost afæculent diarrhœa which followed the exhibition of TEM to two patients in the terminal stages of their disease (Cases 16 and 19). This same type of diarrhœa has been produced experimentally in rats and dogs (Philips and Thiersch, 1950), and we regard it as a very serious toxic effect and of grave prognosis.

Resistance to Infection.

One of our patients (Case 30) died with lobar pneumonia twenty-six days after being given TEM. There was little pyrexia and no leucocytosis, and the disease ran an

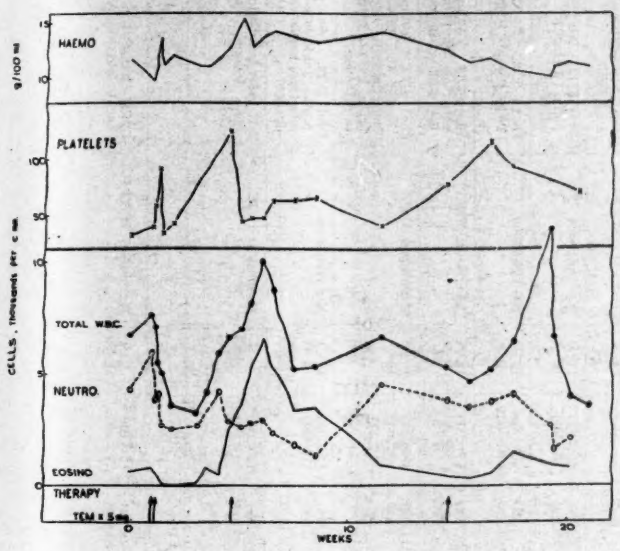

FIGURE IV.

Case 34. Graph showing example of the eosinophilic response to TEM.

atypical course. In a second patient (Case 10), who died two weeks after the last dose, autopsy revealed a psoas abscess without bony lesion. Here again there was no

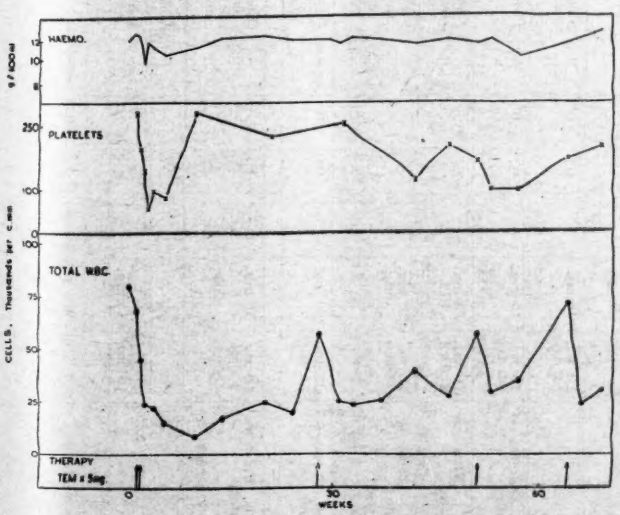

FIGURE V.

Case 14. Graph showing typical response of lymphocytes and behaviour of the platelets in a patient with chronic lymphocytic leuchæmia. Satisfactory control over a long period.

leucocytosis. The lack of response of the leucocytes, depressed by TEM, may have been responsible for failure of resistance. There is some evidence also that actual antibody formation may be depressed by this type of drug (Chasis, Goldring and Baldwin, 1949; Jacobson *et alii*, 1949). On the other hand, in another case, chronic pulmonary tuberculosis was quite unaffected (Case 2).

Vascular Effects.

In Case 16 generalized increase in capillary permeability appeared to have been caused by the drug, and death occurred fifteen days after a small dose of TEM. Terminally there was a rapid onset of widespread œdema, pulmonary œdema, severe, watery diarrhœa, and epileptiform convulsions. *The cerebro-spinal fluid pressure was raised.* At autopsy all tissues were œdematous.

PATHOLOGY.

In those instances in which TEM may have produced *detrimental effects the autopsy material was critically* reviewed. There were no constant pathological changes, but the following were noted: reduction of hæmatopoietic elements in the bone marrow, *fibrinoid arteritis in the* kidney, dilatation of Bowman's capsule and minimal *tubular damage, toxic liver changes with slight fibrosis,* changes in the pancreas consistent with uræmia, cerebral œdema and nerve cell damage. These isolated observations *are noted briefly, and their relationship to TEM therapy is* not clear. They will be the subject of a further report in a subsequent paper.

CASES.

Hodgkin's Disease.

For Hodgkin's disease (Table I) we have adopted the following clinical classification,[1] modified from Karnofsky (1951). This grading assists greatly in gauging the prognosis, the amount of treatment possible and the likely *response. Stage I: Patients with one gland group affected.* Stage II: Patients with more than one gland group affected, but in good condition and with no constitutional symptoms. *Stage III: Patients with widespread disease* and constitutional symptoms, but still in fairly good condition. Stage IV: Patients with widespread disease and constitutional symptoms, but in poor general condition.

We have treated a total of 12 patients grouped as follows: none in Stage I, one in Stage II, four in Stage III and seven in Stage IV.

Stages I and II.

From other reports (Karnofsky *et alii*, 1951; Rundles and Barton, 1952) we have accepted that these stages of Hodgkin's disease are best treated by radiotherapy. One *single patient with Stage II disease (Case 1) was accepted* because of intense pruritus, which responded well. She has since been managed by radiotherapy.

Stages III and IV.

Of our four patients in Stage III, two responded well and one fairly well, and one was probably harmed by too vigorous treatment. In Stage IV, among seven patients, there were one good response and three satisfactory but short remissions. In two cases there was no effect, and *in the seventh death was probably hastened by injudicious* dosage.

The usual response was thus favourable. Resistance to radiotherapy did not necessarily mean resistance to TEM, and there was no constant correlation between the two. As would be expected, remissions induced in patients with Stage IV disease were not so long or so complete as in Stage III. *The response to the initial dose was invariably* more satisfactory than to subsequent doses.

General symptoms such as fever and malaise quickly abated, and most patients noticed rapid subjective improvement. Superficial lymph nodes became smaller, softer and more diffuse and often disappeared completely, usually within four weeks. The internal glands (abdominal, mediastinal) responded as efficiently only in two cases (Cases 2 and 12). Enlargement of the liver was reduced moderately, and enlargement of the spleen usually more

[1] This grading was applied also to lymphosarcoma, follicular lymphoma and reticulosarcoma.

TABLE I.

Case No.	Sex; Age; Duration; Stage.	Previous Irradiation.	Dose and Time.		Effect on Disease.[1]					Effect on Blood.			Clinical Result.	Remarks.
			Initial.	Total.	External Nodes.	Liver and Spleen.	Abdomen.	Hilar Nodes.	Other Changes.	Leucocytes; Maximum and Minimum. (Per Cubic Millimetre.)	Platelets, Maximum and Minimum. (Per Cubic Millimetre.)	Hæmoglobin Value. (Grammes per Centum.)		
Hodgkin's Disease.														
1	F.; 31; 5 years; Stage II.	Yes. None recently.	10 mg. 2 days	10 mg.	+++	–	–	+	Urticaria. Pruritus relieved.	8400 3400	416,000 115,000	10·4 12·2	Remission 10/52.	4/12 later irradiation to mediastinum. Now well, 16/12.
2	F.; 35; 3 years; Stage III.	Much. Neck recently.	15 mg. 5 days	15 mg.	++	–	+++	–	Fever remitted.	17,200 5300	212,000 70,000	9·8 10·2	Remission 32/52.	Quiescent pulmonary tuberculosis unaffected (temporary menstrual irregularity). Now well, 9/12.
3	F.; 51; 4 years; Stage III.	Much. Abdomen recently.	15 mg. 5 days	15 mg.	++	+	++	–	Fever remitted.	8000 500	150,000 3000	10·1 3·3	Remission 3/52.	Died 3/12. No autopsy. Pancytopenia. Excessive dosage. Jaundice, probable hepatitis.
4	M.; 27; 4 years; Stage III.	Yes. None recently.	10 mg. 2 days	15 mg. 1/12	++	++	++	–	Fever remitted.	7900 3500	309,000 92,000	10·4 8·9	Remission 10/52	Returned to work, but condition now deteriorating. Fairly well, 4/12.
5	M.; 18; 5 years; Stage III.	Much. Thoracic spine recently.	5 mg. 4 days	5 mg.	++	+	–	–	Urticaria.	3300 1200	142,000 52,000	11·6 6·6	Probable remission 10/52.	Died 4/12. Autopsy. Hodgkin's disease and unsuspected torulosis. Small dose because of leucopenia.
6	M.; 21; 1 month; Stage IV.	—	10 mg. 2 days	15 mg. 8/52	++	+	–	+	Fever remitted.	8000 500	Not recorded.	10·6 8·8	Remission 3/52.	Died 9/52. Autopsy. Surprising but brief response. Recovery of leucopenia.
7	M.; 75; 6 months; Stage IV.	—	10 mg. 14 days	10 mg.	+	0	0	0	Skin infiltration and ascites unchanged.	18,000 13,200	250,000 52,000	11·0 12·1	No remission.	Died 1/12. No autopsy. Eosinophilic response. Disease unaffected.
8	M.; 61; 2 years; Stage IV.	Yes. Abdomen recently.	15 mg. 14 days	15 mg.	+	0	0	0	Fever unaffected.	7400 3200	Always abundant.	12·0 9·5	No remission.	Died 5/12. No autopsy. Complete lack of response.
9	M.; 28; 2 years; Stage IV.	Yes. None recently.	10 mg. 2 days	15 mg. 1/12	++	++	–	–	Fever remitted. Pulmonary infiltration cleared.	30,000 1300	170,000 76,000	14·6 8·9	Remission 3/52.	Died 4/12. Autopsy. Complete reduction of pulmonary infiltration and eosinophilia.
10	M.; 64; 2 years; Stage IV.	Yes. Groin recently.	15 mg. 3 days	20 mg. 3/12	+	++	+	+	Pleural effusion controlled.	14,300 1500	189,000 52,000	13·0 12·0	Remission 4/52.	Died 4/12. Autopsy. Hodgkin's disease and psoas abscess (non-tuberculous). Recovery of leucopenia, but poor leucocyte response to infection.
11	M.; 37; 6 years; Stage IV.	Much. Thorax recently.	20 mg. 15 days	20 mg.	+	0	0	0	Fever unaffected. Pulmonary infiltration unchanged.	19,000 1300	135,000 8000	12·5 5·0	No remission.	Died 2/12. Autopsy. Pancytopenia. Toxic hepatitis and gastro-intestinal hæmorrhage. Excessive dosage.
12	F.; 30; 7 years; Stage IV.	Much. Pelvis recently.	10 mg. 2 days	10 mg.	–	–	+++	–	Œdema of legs and intestinal obstruction relieved. Pleural effusion controlled.	18,500 7100	175,000 44,000	7·4 10·6	Remission 11/52.	3/12 later irradiation to unaffected bone lesions. Now fairly well, 12/12.
Chronic Lymphocytic Leuchæmia.														
13	M.; 78; 2 years.	—	10 mg. 3/52	15 mg. 4/12	++	+	–	–	—	131,000 25,000	70,000 17,000	9·7 11·5	Remission 14/52+.	Initial transfusion. Good subsequent control. Now well, 6/12.

[1] "+++", complete resolution; "++", marked regression; "+", slight regression; "0", no change; "–", area not involved.

TABLE I.—*Continued.*

Case No.	Sex; Age; Duration; Stage.	Previous Irradiation.	Dose and Time.		Effect on Disease.[1]					Effect on Blood.			Clinical Result.	Remarks.
			Initial.	Total.	External Nodes.	Liver and Spleen.	Abdomen.	Hilar Nodes.	Other Changes.	Leucocytes; Maximum and Minimum. (Per Cubic Millimetre.)	Platelets, Maximum and Minimum. (Per Cubic Millimetre.)	Hæmoglobin Value. (Grammes per Centum.)		
									Chronic Lymphocytic Leuchaemia.—Continued.					
14	F.; 74; 4 years.	Much. None recently.	10 mg. 2 days	20 mg. 6/12	+++	++	−	−	Dysphagia relieved. Urticaria.	80,000 9100	270,000 50,000	9·7 12·4	Remission 22/52.	Extreme nausea. Relief of dysphagia with rising hæmoglobin value. Controlled by intermittent doses. Well, 18/12.
15	M.; 78; 18 months.	Much. Axilla recently.	10 mg. 2 days	10 mg.	+++	−	−	−	——	11,200 1800	139,000 54,000	10·3 13·0	Remission 26/52.	Died 7/12. Abrupt febrile illness. Poor leucocyte response. Autopsy: impetigo, purulent bronchitis.
16	M.; 33; Indefinite.	—	10 mg. 2 days	25 mg. 7/12	++	++	+	−	——	21,000 4200	154,000 72,000	11·8 13·1	Remission 22/52.	Died 8/12. Autopsy. Eventual toxicity, convulsions, œdema, watery diarrhœa.
17	M.; 61; 1 year.	—	10 mg. 4 days	10 mg.	0	0	0	−	——	22,300 4200	110,000 36,000	12·4 9·7	No remission.	Surprising lack of response. Irradiation 2/12 later with improvement. Now alive but ill, 5/12.
18	M.; 54; 6 years.	Much. None recently.	5 mg. 1 day	20 mg. 7/12	+	+	+	−	——	73,000 26,100	35,000 61,000	13·6 16·4	Remission 8/52.	Leuchæmia overshadowed by bronchitis and emphysema. Satisfactory control. Now fairly well, 9/12.
19	M.; 74; 5 years.	Much. Spleen recently.	10 mg. 3 days	22·5 mg. 8/12	++	++	+	−	Skin infiltration resolved.	106,000 15,300	69,000 18,000	10·1 7·1	Remission 12/52.	Died 9/12. No autopsy. Terminal disease well controlled. Eventual toxicity (watery diarrhœa) from overdosage.
20	M.; 65; 8 months.	—	10 mg. 2 days	10 mg.	0	0	0	—	Oliguria.	740,000 310,000	51,000 40,000	4·2 7·5	No remission.	Died 12 days. Intestinal obstruction. C.C.F. (mercurials). Precipitous fall in leucocytes. Death in uræmia. Autopsy.
21	M.; 38; 2 months.	—	5 mg. 1 day	5 mg.	++	++	−	−	Fever abated.	53,000 600	138,000 24,000	9·3 7·2	Remission 14/52+.	Hyperactive phase. Extreme neutropenia followed by surprising and extending remission. Now well, 6/12.
22	M.; 47; 6 months.	—	10 mg. 2 days	10 mg.	0	0	0	−	Fever unaffected.	192,000 2700	52,000 None	8·6 4·2	No remission.	Died 1/52. Autopsy. Overdosage with disease in hyperactive phase. Absolute thrombocytopenia. Precipitous fall in leucocytes.
									Lymphosarcoma.					
23	F.; 73; 3 months; Stage II.	—	10 mg. 2 days	10 mg.	+++	−	−	−	Œdema of leg relieved.	7600 3100	166,000 72,000	11·0 13·0	Remission 38/52+.	Excellent response. Now well, 10/12.
24	F.; 40; 3 months; Stage II.	—	10 mg. 2 days	15 mg. 1/12	++	−	++	−	Tonsil reduced.	9500 5500	456,000 82,000	13·0 13·3	Remission 4/52+.	Remission commencing. Now well, 3/12.
25	M.; 56; 18 months; Stage II.	—	15 mg. 2 days	30 mg. 6/12	++	−	−	−	——	10,900 3800	300,000 200,000	13·0 13·6	Remission 20/52.	Died 9/12. Autopsy. Widespread bone involvement unaffected. Poor subsequent response.

[1] "+++", complete resolution; "++", marked regression; "+", slight regression; "0", no change; "−", area not involved.

TABLE I.—*Continued.*

Case No.	Sex; Age; Duration; Stage.	Previous Irradiation.	Dose and Time.		Effect on Disease.[1]					Effect on Blood.			Clinical Result.	Remarks.
			Initial.	Total.	External Nodes.	Liver and Spleen.	Abdomen.	Hilar Nodes.	Other Changes.	Leucocytes; Maximum and Minimum. (Per Cubic Millimetre.)	Platelets, Maximum and Minimum. (Per Cubic Millimetre.)	Hæmoglobin Value. (Grammes per Centum.)		
Lymphosarcoma.														
26	M.; 70; 4 months; Stage III.	—	10 mg. 2 days	20 mg. 2/12	0	0	0	—	Marked euphoria. Increased appetite.	10,200 3300	194,000 59,000	10·0 11·0	No remission.	Died 13/12. No autopsy. Unresponsive. Immediate irradiation with good effect.
27	F.; 51; 5 years; Stage III.	Much. None recently.	10 mg. 2 days	10 mg.	+++	—	++	—	Fever remitted.	6000 3200	118,000 59,000	12·0 10·1	Remission 24/52+.	Unusual reduction of abdominal glands. Now well, 7/12.
28	M.; 48; 10 years; Stage III.	Much. None recently.	10 mg. 2 days	10 mg.	—	+	—	—	Subcutaneous tumours resolved. C.N.S. signs improved.	4300 2600	215,000 77,000	12·8 13·0	Objective, but no subjective improvement.	Unusual C.N.S. involvement (nystagmus and third nerve palsy); 1/12 later mental confusion with good response to irradiation. Bone lesions unchanged. Recent pathological fracture. Now fairly well, 10/12.
29	F.; 70; 1 year; Stage IV.	Yes. Mediastinum recently.	2·5 mg. 1 day	2·5 mg.	0	0	0	0	—	54,000 34,000	69,000 9000	9·7 10·4	No remission.	Lymphosarcoma merging into leuchæmia. Treatment abandoned because of thrombocytopenia. Now fairly well, 3/12.
30	F.; 53; 10 years; Stage IV.	Much. None recently.	10 mg. 2 days	10 mg.	—	—	0	—	—	7800 1900	138,000 37,000	13·3 8·1	No remission.	Died 1/12. Autopsy. Lymphosarcoma and lobar pneumonia. Inhibited leucocyte response.
31	M.; 60; Stage IV.	—	10 mg. 2 days	10 mg.	++	+	0	—	Oliguria.	11,200 6400	154,000 90,000	10·1 8·7	No remission.	Died 12 days. No autopsy. Death in uræmia.
Follicular Lymphoma.														
32	M.; 48; 3 months; Stage II.	—	15 mg. 3/52	15 mg.	+++	—	—	—	—	11,000 4500	354,000 219,000	14·0 15·0	Remission 28/52+.	Unassociated hepatomegaly. Now well, 8/12.
33	F.; 24; 2 years; Stage III.	—	10 mg. 2 days	10 mg.	++	++	—	—	—	No significant fall		7·0 11·2	Remission 26/52+.	Correction of severe anæmia. Now well, 8/12.
34	M.; 43; 2 years; Stage III.	Much. Abdomen recently.	15 mg. 3/52	20 mg. 3/12	++	++	+	—	Eosinophilia.	7600 3300	90,000 30,000	11·2 14·1	Remission 12/52.	Previous nitrogen mustard. Subsequent irradiation. Persistent leucopenia and thrombocytopenia. Now fairly well, 18/12.
Reticulosarcoma.														
35	F.; 43; 2 months; Stage III.	—	10 mg. 4 days	10 mg.	++	—	++	—	—	14,600 4200	310,000 120,000	11·7 12·4	Remission 6/52.	Marked improvement, allowing abdominal irradiation. Now well, 4/12.
36	F.; 58; 5 months; Stage IV.	—	15 mg. 12 days	15 mg.	0	0	0	0	Fever and pleural effusion unchanged.	9000 3200	192,000 71,000	9·3 8·1	No remission.	Died 4/12. No autopsy. Complete lack of response.
37	F.; 53; 3 years; Stage IV.	—	10 mg. 2 days	10 mg.	++	0	—	—	Pain relieved. Bone lesions unchanged.	No significant fall.			Remission 3/52.	Died 2/12. No autopsy. Fungation of glands prevented. Dramatic relief of pain.

[1] "+++", complete resolution; "++", marked regression; "+", slight regression; "0", no change; "—", area not involved.

TABLE I.—*Continued.*

Case No.	Sex; Age; Duration; Stage.	Previous Irradiation.	Dose and Time.		Effect on Disease.[1]					Effect on Blood.			Clinical Result.	Remarks.
			Initial.	Total.	External Nodes.	Liver and Spleen.	Abdomen.	Hilar Nodes.	Other Changes.	Leucocytes; Maximum and Minimum. (Per Cubic Millimetre.)	Platelets, Maximum and Minimum. (Per Cubic Millimetre.)	Haemoglobin Value. (Grammes per Centum.)		
								Polycythæmia Vera.						
38	M.; 60; 7 years.	Yes, consly. None re-	15 mg. 14 days	25 mg. 6/52	—	++	—	—	—	8800 8300	185,000 68,000	21·6 12·0	Remission 6/52+.	Delayed but satisfactory response. Now well, 5/12.
								Löffler's Disease.						
40	F.; 34; 5 years.	—	10 mg. 8 days	10 mg.	—	—	—	—	Considerable radiological clearing.	13,100 5000	160,000 52,000	13·8 12·2	Not yet determined.	Eosinophile cells falling satisfactorily. Too early for full assessment. Now well, 2/12.
								Malignant Melanoma.						
41	M.; 22; 18 months.	—	15 mg. 8 days	15 mg.	0	—	—	—	—	6900 5200	173,000 140,000	13·4 13·0	No remission.	No response. Minimal effect on blood count. Now widespread disease. Alive, 6/12.
42	M.; 33; 6 years.	Yes, consly. None re-	15 mg. 3 days	15 mg.	—	—	0	—	Ascites unchanged.	17,000 7600	185,000 70,000	12·0 10·8	No remission.	Died 2/12. No autopsy. No response as expected. Minimal effect on blood count.

[1] "++++", complete resolution; "+++", marked regression; "++", slight regression; "0", no change; "—", area not involved.

completely, but neither organ returned to normal size. Pulmonary infiltration with Hodgkin's tissue occurred in two instances (Case 9 and 11), in one (Case 9, Figures VI and VII) becoming noticeably more extensive before commencing to recede. This type of reaction may indicate a danger in using TEM when obstructive symptoms are present. We were impressed with the control of pleural effusion which, when once aspirated, did not quickly return (Cases 10 and 12). In no case were bone lesions affected. One patient with skin involvement was quite unresponsive to treatment.

Dosage.

The Stage II patient was given 10 milligrammes initially. The initial dose in Stage III varied from five to fifteen milligrammes, and one patient was harmed by 15 milligrammes. In Stage IV the initial dose was 10 to 20 milligrammes, and one patient was harmed by the 20 milligramme dose. Stage III and IV patients late in this series were given a maximum initial dose of 10 milligrammes. Further doses were delayed as long as possible until the granulocytes and thrombocytes had recovered and the remission had completely terminated; these doses did not exceed five milligrammes. No true regular maintenance therapy was attempted.

Chronic Lymphocytic Leuchæmia.

We have treated 10 patients with chronic lymphocytic leuchæmia; four had been given much radiotherapy in the past, and six had received no previous treatment. Good results were obtained in seven, four of whom are still alive and under the same treatment (Table I). One deserves special mention (Case 21). This man, with chronic lymphocytic leuchæmia, was in an extremely active phase with universally enlarged glands, severe anæmia and pyrexia. A dose of five milligrammes caused severe lymphopenia and a profound and almost total neutropenia, which persisted for three weeks and required many transfusions and antibiotics; but he eventually recovered. A complete remission of more than four months followed (Figure VIII). The three patients who derived no benefit came from the previously untreated group. In one (Case 17) examination of the peripheral blood indicated satisfactory absorption, but the glands were reduced only slightly and there was a complete and surprising absence of clinical response; the second patient (Case 20) presented a complicated problem, and a bad result was almost inevitable; the third, like the patient in Case 21, was in an active phase and was harmed by a 10 milligramme dose (Case 22).

The usual pattern of response was pronounced subjective improvement, quick reduction in superficial lymph glands (Figures IX and X), slower and less complete reduction in the internal glands and a good partial response of the enlarged liver and spleen. Maximum regression occurred within four weeks. In one patient leuchæmic skin infiltration rapidly disappeared (Case 19). The total leucocyte count invariably fell sharply (Figure V), and although this was mainly at the expense of the lymphocytes, the number of granulocytes also fell. In five patients there was a significant rise in hæmoglobin value as the leucocytes were brought under control. The response of the lymphoid tissue was greatest to the initial dose and less complete to subsequent ones. Nevertheless control was possible for extended periods, and the numbers of leucocytes continued to fall sharply after each dose.

Dosage: Later patients were given five milligrammes initially, as a review of our earlier material showed a precipitous and sometimes dangerous fall of leucocytes with larger doses (Figure XI). Further small amounts (2·5 to 5·0 milligrammes) were given when increasing lymphocytes, enlarging glands and a return of constitutional symptoms indicated that the remission had ended (Figure V). Small intermittent doses allowed satisfactory management. True maintenance treatment was not attempted.

Lymphosarcoma.

With regard to lymphosarcoma (Table I), we agree with the concept so ably emphasized by Willis (1953) of the close relationship between lymphosarcoma and chronic

lymphocytic leuchæmia, the only distinction being the circulating metastases which constitute leuchæmia. In spite of their similarity there was a significant difference in this series in their behaviour to TEM. Considering the excellent results obtained in chronic lymphocytic leuchæmia, our results in nine cases were unpredictable and at times disappointing. The clinical response was

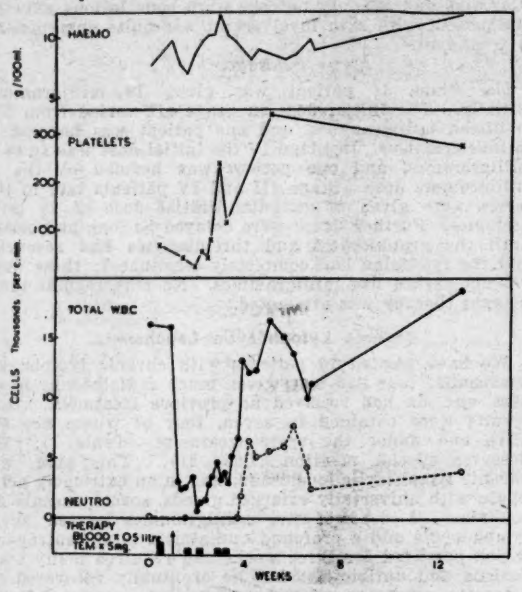

FIGURE VIII.

Case 21. Graph showing the hæmatological changes in active chronic lymphocytic leuchæmia following a small dose of TEM.

excellent in two cases, good in two others and nil in four, in two of which TEM therapy was the initial treatment. The final patient (Case 28) presented an involved problem, and no true clinical remission occurred. In most instances, glandular, splenic and hepatic enlargement responded in the same way as in Hodgkin's disease. In various patients, large skin nodules disappeared completely (Figures XII and XIII); an enlarged tonsil returned to normal size; a radiologically obvious filling defect in the stomach (presumably lymphosarcomatous) was unchanged; bone lesions were not affected, and indeed in one patient (Case 25) a vertebra collapsed whilst he was enjoying a symptomatic remission.

Dosage: The initial dosage varied from 2·5 to 20 milligrammes. The two best remissions were obtained with 10 milligrammes in each case. Subsequent dosage was arranged as in Hodgkin's disease.

Follicular Lymphoma.

Good remissions in follicular lymphoma (Table I) were produced in all three cases, and the general pattern was the same as in Hodgkin's disease and lymphosarcoma. One patient (Case 34), treated extensively by other means in the past, was tided over a very difficult period. The other two had not had previous specific therapy, and lasting improvement occurred. Eosinophilia was caused by the drug in one case. Hæmoglobin values improved coincidently with general improvement in two cases. No serious toxic symptoms were seen. The initial dosage varied from 10 to 15 milligrammes.

Reticulosarcoma.

Three patients suffering from reticulosarcoma were treated with poor results, real benefit being obtained only in one (Table I). The initial dosage was 10 or 15 milligrammes.

Other Diseases.

In addition, the following conditions have been treated (Table I): *polycythæmia vera* (one case), Löffler's syndrome (one case), and malignant melanoma (two cases). The results in polycythæmia, a higher dosage being used than in the reticuloses, appear promising. The patient with Löffler's syndrome was selected for trial because of the dramatic response of pulmonary infiltration and eosinophilia in Hodgkin's disease. The result was inconclusive. The two patients with malignant melanoma derived no benefit.

Discussion.

TEM has had short but intensive use, and many reports have emphasized its toxicity and unpredictable action. It is, therefore, important to decide whether its use has any therapeutic justification, and if so, to define its position and how it can be used safely. A drug which can be given orally has considerable advantages and should not be discarded lightly. The present investigation shows that TEM, although not an ideal substance, still holds a valuable place in the treatment of the neoplastic disorders of hæmatopoietic tissue.

The efficacy of TEM is widely accepted, but its toxicity has proved a serious deterrent. The bone marrow is the most sensitive tissue, and bone marrow depression is a direct and consistent result of excessive dosage. A variety of other serious toxic effects have also occurred. Meyer *et alii* (1952) state that bone marrow vulnerability is unpredictable, and other authors have emphasized the marrow margin between therapeutic and toxic doses (Axelrod *et alii*, 1953; Pavlovsky and Vileseca, 1953; Gellhorn, Kligerman and Jaffe, 1952). In some centres the drug has been abandoned. However, the conditions in which it may be dangerously toxic can be defined and hence avoided.

Our investigation has again proved that when it is given orally, with preliminary alkalinization to the fasting patient, absorption is constant and small doses are effective. This avoids the difficult position of unpredictable absorption which made earlier reports so inconsistent, and was sometimes responsible for overdosage. Enteric-coated tablets, suggested by Paterson, Kunkler and Walpole (1953), are not necessary. In the malignant lymphoid diseases the liability to toxicity to TEM is closely bound

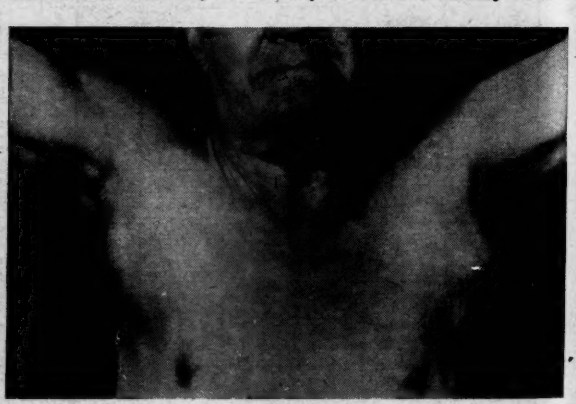

FIGURE IX.

Case 15. Illustrating resolution of axillary glands.

up with the patient's physical state, with the extent of the disease and its aggressiveness, with the amount and timing of previous treatment, and with the presence of neutropenia and thrombocytopenia. As the disease progresses the general condition tends to deteriorate, and most important, there is increasing depression of bone marrow, with diminished powers of recovery. Early stages can be safely treated by TEM, later stages require increasing care and smaller doses, while in the terminal stages only very small doses should be given, with extreme

caution and with full use of supportive measures when necessary. In advanced cases it is difficult to give any effective dose safely, and the drug is generally contra-indicated. Severe neutropenia or thrombocytopenia entirely

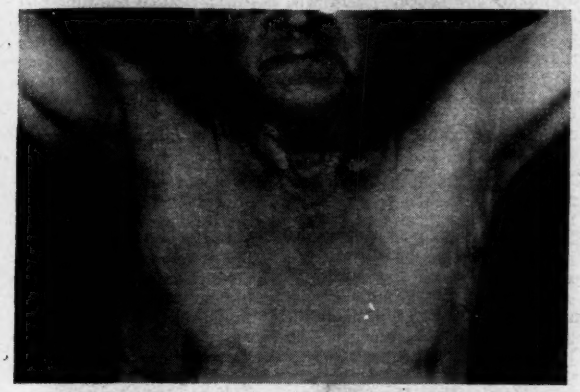

FIGURE X.
Case 15. Illustrating resolution of axillary glands.

precludes its use, and it should always be abandoned if moderate leucopenia is produced without clinical amelioration. If these facts are heeded, serious toxicity can be avoided. On the other hand, in diseases not directly involving the hæmatopoietic system such as malignant melanoma, and in polycythæmia with its plethora of cells, the marrow is much less sensitive to TEM.

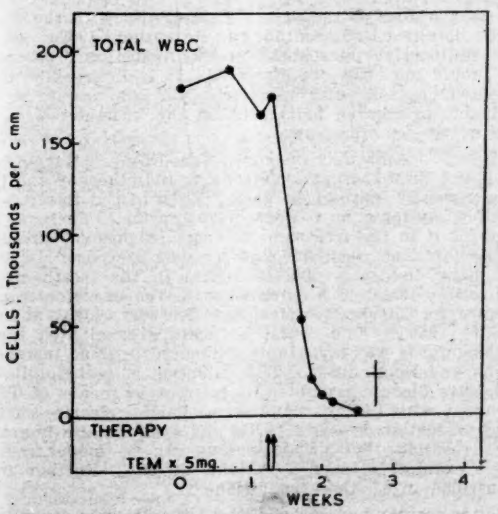

FIGURE XI.
Case 22. Graph showing extreme sensitivity and fatal depression of the leucocytes.

Various ways of reducing toxicity without altering the therapeutic effectiveness have been suggested. Wright *et alii* (1952) used L-cysteine and the citrovorum factor. Cysteine was also used by Weisenberger, Heinle and Levine (1951) to prevent the leucopenia normally caused by nitrogen mustard. These reports are not convincing. Minor toxicity, mainly nausea and vomiting, has been reduced by "Luminal" and by pyridoxine (Wright *et alii*, 1952). We find these symptoms of no great consequence with the low dosage used; they are mostly avoided by the patient's resting on the day when the drug is taken.

TEM gives its best results in chronic lymphocytic leuchæmia. The malignant lymphocyte is extraordinarily sensitive, and lymphoid masses and lymphocytes in the blood are reduced rapidly with very small doses. A satisfactory response can usually be expected, and administration of TEM is often the treatment of choice. The natural course of this disease is one of increasing lymphopoiesis and increasing infiltration of the marrow, causing anæmia and thrombocytopenia in the later stages. It can be slowed by keeping the total leucocyte count at approximately 20,000 per cubic millimetre, and this can usually be accomplished by intermittent doses of TEM. At this level, symptoms are controlled, hæmatopoiesis and thrombopoiesis are not depressed by crowding, and there are enough granulocytes to combat infection. For the subject in good physical condition whose disease is set at a slow inherent *tempo*, and with prominent peripheral glands and minimal abdominal signs, TEM therapy is the best available. Splenomegaly, hepatomegaly and abdominal lymphadenopathy do not respond as well. Hence, when there is isolated enlargement of the spleen, or when enlargement of the liver and abdominal lymphatic glands is also present, radiotherapy should be used. Local pressure or signs of obstruction call for irradiation. Reduced renal function demands cautious treatment because of the very real danger of uræmia, and it is unwise to give mercurial

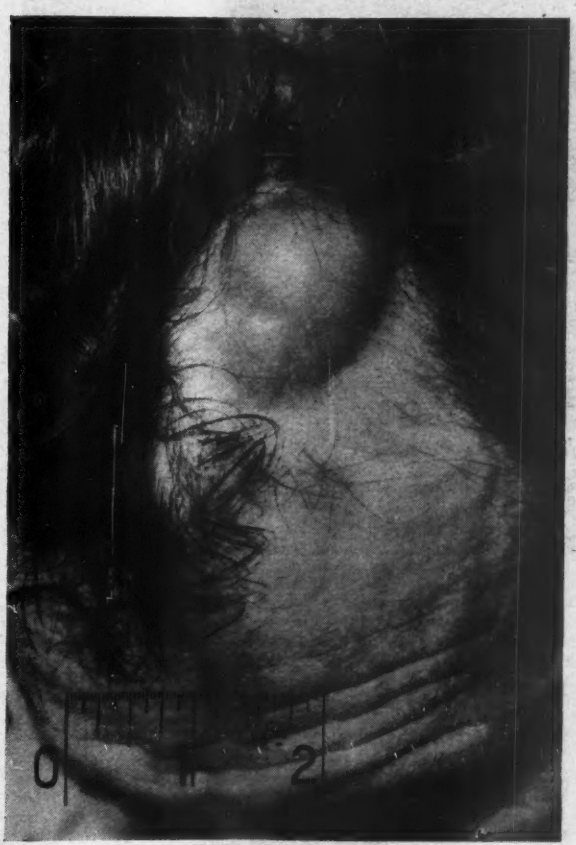

FIGURE XII.
Case 28. Illustrating resolution of lymphosarcomatous deposits in the skin of the scalp.

diuretics while TEM is acting. As the disease advances and the physical condition deteriorates or the pace quickens, poorer results are obtained with any therapy, and late disease is always difficult to manage. If the patient has been previously untreated, cautious splenic irradiation

gives greater control over the fall in leucocytes. However, many patients in the terminal stages (all of ours) have been irradiated to the point of no response, and for these TEM administration is the treatment of choice. It is superior to nitrogen mustard, and constitutional symptoms are slight.

In Hodgkin's disease and lymphosarcoma results with TEM are good, but in general inferior to those obtained in chronic lymphocytic leuchæmia. In follicular lymphoma remissions were obtained in our three cases; but this probably reflects to some extent the slow natural course of the disease. Results also vary considerably according to the stage of the disease, and a system of grading is highly important. Radiotherapy is commonly used in Stage I disease, almost invariably with good effect (Slaughter and Craver, 1942; Peters, 1950). The very occasional reports of cure have occurred in patients of this type who have had local treatment by irradiation, surgical excision or a combination of the two (Baker and Mann, 1940; Gall, 1943; Jackson and Parker, 1946; Hellwig, 1947). Work has recently appeared suggesting that local therapy combined with some form of total body irradiation may give better results (Medinger and Craver, 1952). This has been an attractive hypothesis for many years; but until it is satisfactorily proved, we see no reason for using a generally acting drug in localized disease. The shrinkage of glands under radiotherapy is more certain, more complete and longer lasting than with TEM. Therefore, Stage II patients with few gland groups affected can comfortably be treated by irradiation with a fairly sure result, and should be treated in this way. TEM therapy is indicated at this stage only in two circumstances: if four or more different areas are affected it may be given first, and then residual masses, if any, irradiated; or if glands have again become enlarged and there is radio-resistance or doubt about skin tolerance to X rays, TEM may be given as substitute therapy, and will at least reduce the amount of irradiation eventually required. Stage II patients are in good condition, the bone marrow is still resilient, the margin of safety is fairly wide, and there is little danger of serious hæmatological toxicity. Equivalent results can be obtained with nitrogen mustard, but it is inconvenient to give, and more often has unpleasant side effects. The toxicity is probably less; but toxicity is no great hazard at this stage.

FIGURE XIII.

Case 28. Illustrating resolution of lymphosarcomatous deposits in the skin of the scalp.

As these diseases become more widespread and as constitutional symptoms appear, TEM becomes therapeutically more important, and we have had better results with it in Stage III disease than with radiotherapy or nitrogen mustard. It has been said (Conley, 1952) that nitrogen mustard is the more effective and less toxic drug; but a comparison of equivalent series of our own patients at this stage was significantly in favour of TEM. Good general physical condition and reasonable marrow function ensure moderate safety. The terminal stages of these diseases are difficult to view with patience. It is essential to recognize that the aim of therapy is to control symptoms and to prolong life. It is a great temptation to treat the patient vigorously in the hope of loosening the generalized hold of the disease, but vigorous treatment of any sort (and TEM is no exception) will invoke a series of complications more distressing than the disease itself, and will hasten the inevitable fatal termination. The difficulty is, that in avoiding toxicity, it is virtually impossible to give an effective dose, and we believe that nitrogen mustard has a wider margin of safety and should be used in preference. Fractional doses of radiotherapy also have a definite place.

A single patient with *polycythæmia vera* responded well to a larger dose of the drug. This agrees with the good results obtained by Rosenthal and Rosenthal (1952). However, radioactive phosphorus is established and effective and should not easily be displaced. In a disease like this in which aplasia and myelosclerosis can occur, it is justifiable to reserve judgement on the ultimate effect of TEM on the bone marrow.

Myeloid leuchæmia responds favourably (Karnofsky, 1951), but TEM therapy is inferior to radiotherapy and the more recently developed drug "Myleran". Results in multiple myeloma have been disappointing. There is no place for it in the treatment of acute leuchæmia. Results in disseminated carcinoma and sarcoma are poor. In non-malignant disease a trial is logical in the treatment of nephrotic œdema, in accordance with the use of nitrogen mustard by Chasis, Goldring and Baldwin (1949) and by Taylor (1950). The course of acute disseminated *lupus erythematosus* was favourably influenced in some instances (Rohn and Bond, 1953). The reduction of eosinophilia in Hodgkin's disease prompted us to treat by means of TEM a woman with Löffler's syndrome. Partial clearing of the lungs, reduction in eosinophilia and symptomatic improvement resulted; but no deductions can be made from a single example of such a variable disease. Further trial is justified in all these conditions.

Better results are obtained in all the diseases considered when the therapeutic weapons are used in a flexible way as the stage and type of the disease indicate, rather than by rigid adherence to one form of treatment from the commencement to the conclusion of the illness. Thus TEM can be aligned with radiotherapy, nitrogen mustard, cortisone, urethane, folic acid antagonists and radioactive phosphorus. If the overall picture is considered, there are stages in some of these diseases when its administration is the treatment of election, and equally other times when it is absolutely contraindicated.

SUMMARY.

1. The results of the treatment with TEM of 41 patients have been presented. The majority suffered from Hodgkin's disease, chronic lymphocytic leuchæmia or lymphosarcoma.

A few patients with follicular lymphoma, reticulosarcoma, *polycythæmia vera*, malignant melanoma and Löffler's syndrome were also treated. The investigation extended over a period of eighteen months.

2. TEM proved of most value in chronic lymphocytic leuchæmia, in Stage II of the malignant lymphoid diseases (but it was not the treatment of choice), in Stage III of these diseases, and in *polycythæmia vera*. It was of limited value in Stage IV disease, and its efficacy was directly related to the patient's general physical condition.

3. It has been found possible to use a lower dose than generally reported. This is attributed to giving the drug to the fasting patient with preliminary alkali, thus ensuring constant absorption.

4. The hæmatological effects were most pronounced on neutrophile cells, platelets and the malignant lymphocytes.

5. Toxic effects have been observed in the bone marrow, the liver, and the gastro-intestinal, renal and central nervous systems, together with minor skin eruptions. The drug is dangerous to patients in poor physical condition. Toxicity can be avoided by careful clinical selection.

6. The relationship of TEM to other agents used in the treatment of the malignant lymphoid diseases has been discussed. It is worthy of further trial in the treatment of nephrotic œdema, *lupus erythematosus* and Löffler's syndrome.

ACKNOWLEDGEMENTS.

We wish to thank the members of the honorary medical staff of Sydney Hospital for their permission to examine, treat and cite many of the patients included in this report; Dr. Sylvia Bray, radiotherapist, for her constant cooperation; and Dr. E. Hirst for reviewing the autopsy material. The TEM used was provided through the courtesy of Lederle Laboratories.

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Legends to Illustrations.

FIGURE VI.—Case 9. X-ray picture showing clearing of Hodgkin's deposits in the lung parenchyma.

FIGURE VII.—Case 9. X-ray picture showing clearing of Hodgkin's deposits in the lung parenchyma.

HÆMOLYTIC ANÆMIA IN HÆMOPHILUS INFLUENZÆ MENINGITIS TREATED WITH SPECIFIC RABBIT SERUM.

By J. MARGOLIS,

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IN the second half of 1952 attention was drawn to severe anæmia, apparently hæmolytic in nature, which developed in a large proportion of patients with *Hæmophilus influenzæ* type B meningitis soon after their admission to the hospital.

Since some of these patients presented with a history of several days, sometimes weeks, of illness, and since it was inconceivable that the rapid fall in hæmoglobin value could have been continuing for long before hospitalization, the necessity of investigating their initial hæmoglobin levels on admission to hospital was obvious. A survey of records of similar patients for the past few years, whilst generally confirming the impression that severe anæmia did, in fact, often develop during their stay in the hospital, was not of great assistance in critical analysis, firstly because the data were far too scanty, secondly because of the changes in treatment and in prognosis during that period.

An intensive study of all future patients was therefore undertaken with a view to establishing the course and if possible the cause of the anæmia, and it soon became apparent that the presence of infection was not sufficient to account for its dramatic onset and course, and that other precipitating factors must be sought.

Attention was soon focused on the use of specific rabbit serum in massive doses (up to 2% of the patient's body weight) as a distinguishing feature in the management of these patients. A relatively high content of human hæmagglutinins was found in the serum used, and this furnished a tentative hypothesis on which to base further investigations.

Clinical Material.

Forty-seven consecutive patients with *H. influenzæ* meningitis admitted to the Royal Alexandra Hospital for Children between October, 1952, and November, 1954, were investigated. All cases were bacteriologically proven except Case 20, in which the diagnosis was reacheed on clinical grounds alone. This case is not included in the analysis of over-all results. For details of management the reader is referred to an earlier paper (Beveridge, 1954). Briefly, all patients received standard treatment with sulphadiazine, streptomycin and chloramphenicol, and, until the latter part of 1953, specific rabbit antiserum given with hyaluronidase, by intramuscular injection in quantities of 90 to 120 millilitres, depending on the size of the child (group I, Table I). In accordance with the example of American workers (Ross *et alii*, 1952; Alexander, 1952), the routine serum treatment was abandoned at that time and, apart from a small overlap, the latter half of this series received no rabbit serum (group III, Table I).

Between July and September, 1953, five unselected patients were given rabbit serum of the same batches as in group I, but absorbed with human red cells to remove the hæmagglutinins present (group II, Table I).

Finally, group IV consists of three patients treated in the second half of 1954. A new batch of serum, which differed greatly in agglutinin content from the previous ones, was used. For this reason, and also because these were no longer unselected cases, they cannot be included in any of the previous groups, and must be considered separately.

Methods.

Hæmoglobin value was estimated in finger-prick blood with a grey wedge photometer. Reticulocytes were counted by a wet preparation method (isotonic solution of brilliant cresyl blue). Osmotic and incubation fragility were measured by standard methods (compare Dacie, 1954). Mechanical fragility tests were performed by a modification of the method described by Shen, Castle and Fleming (1944).

Citrated capillary blood, 0·5 millilitre, was rotated for one hour in a vertical plane at 100 revolutions per minute in 50-millilitre Erlenmeyer flasks containing eight glass beads each four millimetres in diameter. The supernatant hæmoglobin was estimated photoelectrically and expressed as percentage hæmolysis. No hæmatocrit adjustment was made. Normal values with this method ranged from 1% to 5%.

Results.

It must be pointed out at the outset that the scope of this investigation was limited by the lack of further clinical material after the abandonment of rabbit serum as a part of the routine treatment. Thus, whilst the later cases provided valuable controls, some of the investigations which were contemplated, such as a more extensive study of mechanical fragility, anti-rabbit globulin tests and estimation of erythrocyte survival times, had to be abandoned. Nevertheless, the data gathered seemed to be sufficient to throw some light on the mechanism of anæmia in these children.

"Auto-agglutination."

Within twenty-four hours of receiving rabbit serum injections all patients in group I showed a striking increase in red cell clumping in their whole or citrated blood as compared to that present prior to serum treatment. The behaviour of a drop of blood placed on a slide often compared in degree of aggregation to agglutination with incompatible serum (Figure IIB). The intensity of this phenomenon, moreover, was almost always parallel to the degree of subsequently developing anæmia. On closer examination it was found that this "auto-agglutination" was largely due to greatly increased rouleaux formation. This could be shown by sedimentation rates of normal cells suspended in the patients' plasma and of patients' cells suspended in normal plasma. Nevertheless, even the cells centrifuged from a large volume of saline showed on attempted resuspension some degree of stickiness which, although not strong enough to be classed as agglutination, appears to indicate some change in the surface properties. None of these changes could be found in groups II and III.

Anæmia.

Since all our patients had a normocytic blood picture on admission to hospital, serial hæmoglobin values only are reported, since they are a more accurate index of anæmia than erythrocyte counts. Whenever possible, initial hæmoglobin levels before treatment were recorded, and thereafter serial determinations were made for ten to twenty days. It is appreciated that changes in the state of hydration as well as other considerations introduce some errors, particularly in younger infants, but these objections apply equally to control groups, and they have therefore been disregarded.

It can be seen in Table I that all patients in group I, with the exception of two (Cases 13 and 16) who were given relatively small doses of serum, developed pronounced anæmia. The fall in hæmoglobin value was often dramatic and could reach as much as six grammes *per centum* in the first three days after the patient's admission to hospital, at which stage it was usually interrupted by blood transfusion. After the post-transfusion rise, the hæmoglobin value often fell again sometimes at the original rate; this in some cases necessitated further blood transfusions. Of the 20 patients in group I, 13 required blood transfusion, some requiring more than one, whereas only one patient among the 23 belonging to groups II and III was given a transfusion; that was immediately after his admission to hospital, when his hæmoglobin level was 10 grammes *per centum* (Table I, column 12). The hæmolytic process appeared to continue for some weeks, although it was usually masked by rapid blood regeneration after the first

TABLE I.

Summary of Clinical and Laboratory Data in 47 Cases of Influenzal Meningitis.

Group.	1 Case Number.	2 Date of Admission to Hospital.	3 Sex.	4 Patient's Age.	5 Blood Group and Rh Status.	6 Duration of Illness Before Admission to Hospital. (Days.)	7 Organisms in Cerebro-spinal Fluid.	8 Dose of Rabbit Serum. (Millilitres per Kilogram of Body Weight.)	9 Sphero-cytosis.	10 Initial Hæmo-globin Value. (Grammes *per Centum*.)	11 Lowest Observed Hæmo-globin Value. (Grammes *per Centum*.)	12 Number of Blood Trans-fusions.	13 Total Hæmo-globin Fall. (Grammes *per Centum*.)	14 Highest Reticulo-cyte Count. (*Per Centum*.)	15 Remarks.
Group I: Rabbit serum with high haemagglutinin content.	1	12.10.52	M.	6 months.	AB+	5	Moderate number.	15·0 and 7·5	Present.	7·2	5·6	2	4·5	—	"Initial hæmoglobin", three days after admission.
	2	31.10.52	F.	9 months.	A+	3	Numerous.	15·0	Present.	10·8	7·5	2	11·1	15	Died before observations completed.
	3	13.11.52	F.	14 months.	O+	9	Occasional.	13·0	Present.	9·2	7·8	1	4·1	5	Osmotic fragility 0·52 to 0·28% saline.
	4	27.11.52	M.	3½ years.	O−	7	Occasional.	8·5	Present.	14·5	7·0	1	7·5	5	Osmotic fragility 0·52 to 0·28% saline.
	5	3.12.52	F.	2 years.	—	3	Moderate number.	9·0	Present.	11·5	7·6	0	3·9	15	Osmotic fragility 0·44 to 0·28% saline.
	6	8.12.52	F.	7 months.	O−	2	Numerous.	16·0	Present.	11·5	6·5	1	9·7	15	
	7	8. 4.53	M.	18 months.	AB+	1	Numerous.	9·2	Present.	11·5	8·2	1	5·6	13	Normal osmotic and incubation fragility.
	8	12. 5.53	F.	7 months.	A+	8	Numerous.	10·5	Present.	10·7	7·5	1	7·7	20	
	9	16. 5.53	M.	2½ years.	B+	3	Numerous.	8·8	Present.	13·5	6·0	2	11·5	5	See Figures I, IIA and IIB.
	10	29. 5.53	M.	4 years.	—	1	Moderate number.	6·5	Present.	14·5	8·5	0	6·0	10	
	11	13. 6.53	M.	5½ years.	—	7	Occasional.	6·3	Present.	13·5	8·5	0	5·0	15	
	12	17. 6.53	F.	2 years.	O+	2	Numerous.	10·0	Present.	12·8	8·0	1	4·8	20	
	13	18. 6.53	M.	5 years.	—	1	Numerous.	3·7	Doubtful.	11·7	11·7	0	0·0	4	Note small dose of rabbit serum.
	14	19. 6.53	M.	5 years.	—	1	Numerous.	6·3	Present.	14·0	10·3	0	3·7	7	
	15	6. 7.53	F.	22 months.	—	1	Moderate number.	7·0	Present.	12·5	8·5	0	4·0	20	
	16	10. 7.53	F.	6 years.	—	1	Occasional.	4·6	Doubtful.	13·0	11·2	0	1·8	5	Note small dose of rabbit serum.
	17	11. 7.53	M.	8 months.	O+	20	Occasional.	10·0	Present.	11·5	7·5	1	5·2	5	Urobilinogen +++
	18	10. 8.53	M.	3 years.	A+	1	Numerous.	6·4	Present.	13·0	7·0	1	6·0	12	
	19	8. 3.54	F.	4 months.	A+	3	Numerous.	7·5	Present.	10·5	7·0	2	4·5	8	Mechanical fragility, 20% on tenth and twelfth days.
	20	7. 5.54	M.	4 months.	O+	14	Nil.	12·0	Present.	7·5	7·5	3	3·2	10	Not proven *H. influenzæ* meningitis. Mechanical fragility, 25% on fourth day.
Group II: Rabbit serum as in Group I, but absorbed with human erythrocytes.	21	2. 7.53	F.	11 months.	—	11	Profuse.	11·0	Absent.	10·4	9·5	0	0·9	6	
	22	7. 9.53	M.	18 months.	—	1	Very occasional.	7·5	Absent.	13·5	12·5	0	1·0	1	
	23	19. 9.53	M.	13 months.	—	5	Occasional.	11·0	Absent.	10·5	10·0	0	0·5	3	
	24	22. 9.53	M.	3 months.	—	3	Occasional.	17·0	Absent.	12·5	11·5	0	1·0	5	
	25	29. 9.53	M.	10 months.	—	3	Occasional.	11·0	Absent.	10·0	10·0	0	0·0	3	
Group III. No rabbit serum given	26	20. 9.53	F.	2 years.	—	2	Moderate number.	—	Absent.	12·5	10·0	0	2·5	3	
	27	11.11.53	F.	20 months.	—	2	Profuse.	—	Absent.	11·5	9·0	0	2·5	3	
	28	6. 3.54	M.	3 months.	B+	9	Numerous.	—	Absent.	10·0	10·0	1	0·5	2	Mechanical fragility, 5%.
	29	28. 4.54	M.	7 months.	—	1	Numerous.	—	Absent.	9·5	9·5	0	0·0	—	
	30	24.11.54	M.	6 months.	—	17	Profuse.	—	Absent.	9·6	9·0	0	0·6	4	Mechanical fragility, 1%.

TABLE I.—*Continued.*

Summary of Clinical and Laboratory Data in 47 Cases of Influenzal Meningitis.

Group.	1 Case Number.	2 Date of Admission to Hospital.	3 Sex.	4 Patient's Age.	5 Blood Group and Rh Status.	6 Duration of Illness Before Admission to Hospital. (Days.)	7 Organisms in Cerebro-spinal Fluid.	8 Dose of Rabbit Serum. (Millilitres per Kilogram of Body Weight.)	9 Spherocytosis.	10 Initial Hæmoglobin Value. (Grammes per Centum.)	11 Lowest Observed Hæmoglobin Value. (Grammes per Centum.)	12 Number of Blood Transfusions.	13 Total Hæmoglobin Fall. (Grammes per Centum.)	14 Highest Reticulocyte Count. (Per Centum.)	15 Remarks.
Group III: No rabbit serum given.	31	20. 6.53	M.	7 months.	—	2	Occasional.	—	Absent.	11·0	11·0	0	0·0	—	
	32	20. 7.53	M.	4 years.	—	2	Very occasional.	—	Absent.	11·5	11·5	0	0·0	3	
	33	14. 8.53	M.	5 years.	—	5	Numerous.	—	Absent.	12·5	11·0	0	1·5	2	
	34	8.10.53	F.	2½ years.	—	2	Moderate number.	—	Absent.	12·1	12·1	0	0·0	2	
	35	10.10.53	M.	5½ years.	—	1	Very occasional.	—	Absent.	11·2	11·2	0	0·0	2	
	36	6.11.53	M.	3 years.	—	1	Moderate number.	—	Absent.	12·0	11·5	0	0·5	—	
	37	21. 4.54	F.	3 years.	—	1	Numerous.	—	Absent.	15·0	12·5	0	2·5	2	Mechanical fragility, 1%.
	38	11. 6.54	M.	22 months.	—	1	Occasional.	—	Absent.	11·7	11·7	0	0·0	3	Mechanical fragility, 4%.
	39	1. 7.54	M.	2½ years.	—	3	Numerous.	—	Absent.	11·5	11·5	0	0·0	2·5	Mechanical fragility, 2%.
	40	2. 7.54	M.	3½ years.	—	2	Occasional.	—	Absent.	12·5	12·0	0	0·5	2	Mechanical fragility, 2%.
	41	7. 8.54	M.	3 years.	—	1	Numerous.	—	Absent.	12·3	12·3	0	0·0	1	
	42	8.10.54	F.	2 years.	—	2	Numerous.	—	Absent.	12·0	11·6	0	0·4	1·5	
	43	18.10.54	F.	4 years.	—	2	Occasional.	—	Absent.	14·0	13·0	0	1·0	0·5	
	44	26.11.54	F.	1½ years.	—	2	Numerous.	—	Absent.	12·0	11·0	0	1·0	1	
Rabbit serum (3). (See text.)	45	18. 7.54	M.	6 months.	A+	28	Very occasional.	12·6	Absent.	11·2	11·2	2	2·0	1	Mechanical fragility, 4%.
	46	2. 8.54	F.	5 weeks.	—	1	Numerous.	6·6	Absent.	14·5	11·7	0	2·8	2	Mechanical fragility, 5%.
	47	10. 8.54	F.	9 months.	O—	13	Numerous.	8·8	Absent.	9·5	9·5	1	1·7	0·5	Mechanical fragility, 3%.

ten days. The time sequence of the anæmia as well as other findings is illustrated in Figures IV to XVI, which represent the process in the most instructive cases.

For the purpose of assessment of group differences, the following two criteria were selected: (i) The lowest hæmoglobin value observed (Table I, column 11, and Figure III); this was obviously not the minimal level in the patients who had received transfusions. (ii) The total hæmoglobin fall, including post-transfusion fall (Table I, column 13); this represents the state of affairs more truly. When the initial level was not recorded prior to serum injection, this figure is probably also an underestimate (for example, Case I).

It can be seen that whilst a degree of anæmia existed in many patients in groups II and III, and also in group I on admission to hospital, and this anæmia was probably causally related to the actual infection, it was in no way comparable, either in severity or in its time sequence, with that described above (Table I, Figure III, Figures IV to XVI).

Spherocytosis.

The findings relating to spherocytosis are set out in Table I, column 9. All patients in group I, except the two mentioned above (Cases 13 and 16), developed progressive structural red cell changes, commencing on the third to seventh day after admission to hospital. In dried stained films the cells appeared to become progressively more microspherocytic as the anæmia advanced. A convenient method of direct comparison of progress blood films was used; two films were stuck together face to face with immersion oil, and manipulated in such a manner as to superimpose areas of equal cell spread. A slight focusing adjustment using the high-power lens brings the two layers of cells alternately into view and allows detection of minor changes.

In severe cases the spherocytosis was as pronounced as it is in congenital hæmolytic jaundice (Figures I and IIA).

However, examination of wet preparations of cells, suspended in their own plasma, showed that the decrease in diameter and increase in staining were largely due to a change in the outlines of the erythrocytes, which became bowl-shaped (Figure IIB).

That the surface-to-volume relationship was not altered to the extent suggested by the stained film appearance is shown by normal or only slightly elevated osmotic fragility in the few cases in which this was estimated. Quantitative incubation fragility, a very sensitive index of spherocytosis, was estimated in one case only (Case 7); normal curves were obtained.

Whilst these studies are too few to warrant extended speculations, the fact that it was the unexpected resistance of the spherocytes to hypotonic saline which prompted a closer scrutiny of their shape, adds to the significance of these findings. As shown in Table I, in none of the cases in the other groups did any structural erythrocyte changes develop.

Mechanical Fragility.

The findings in relation to mechanical fragility are shown in Table I, column 15.

Unfortunately this method of investigation was not applied until towards the end

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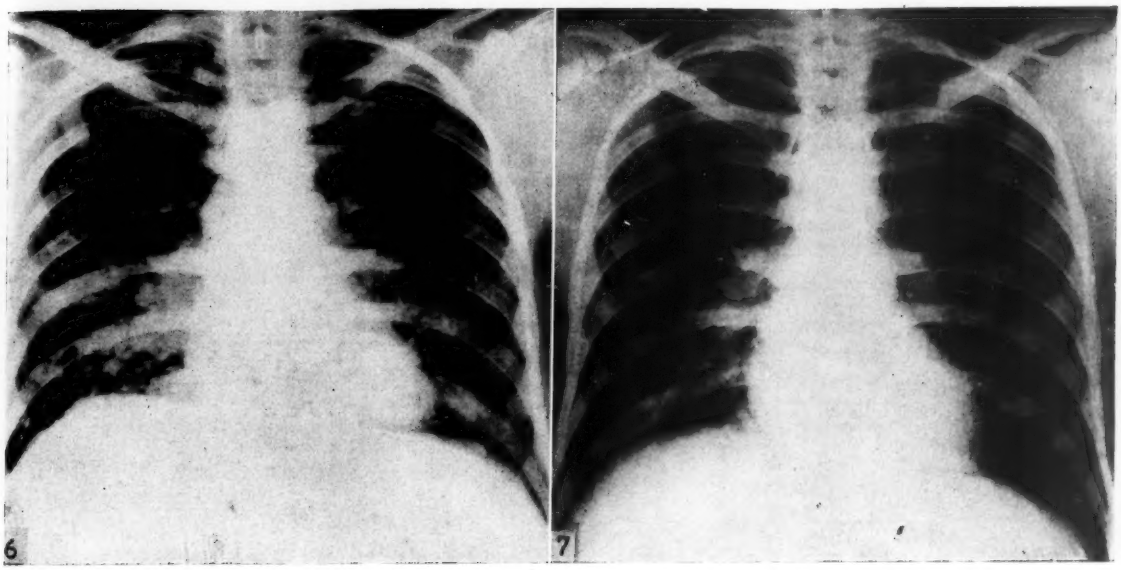

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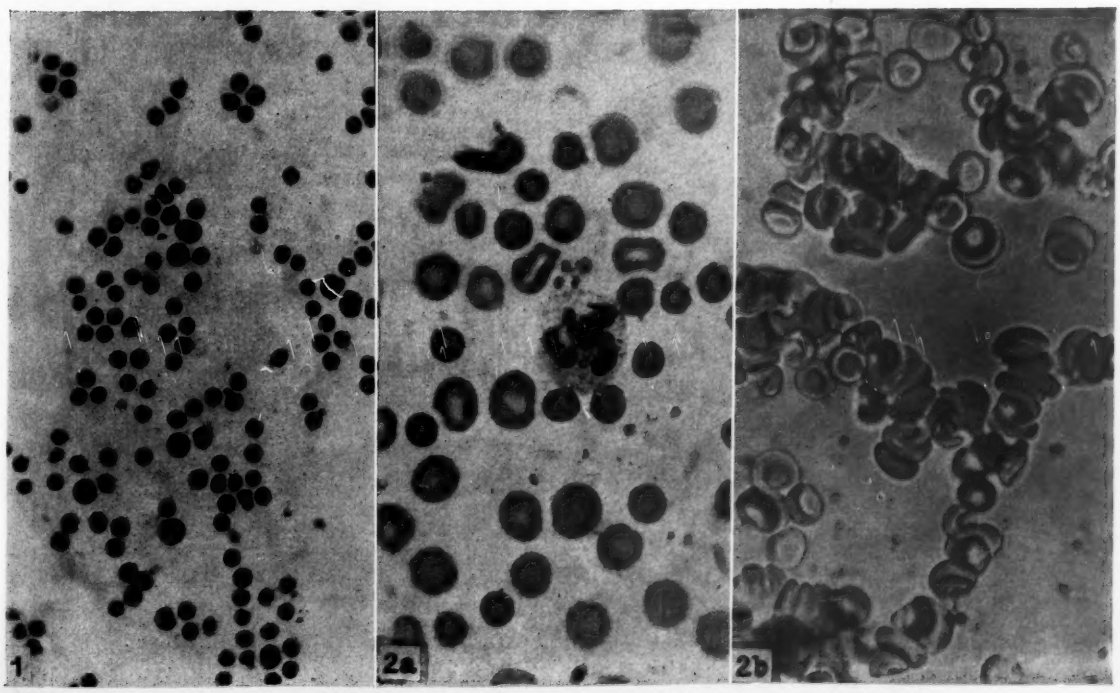

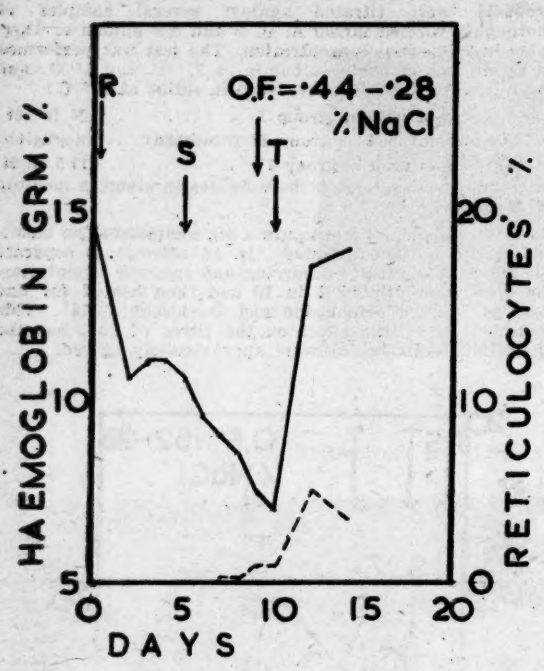

FIGURE V: Case 4.

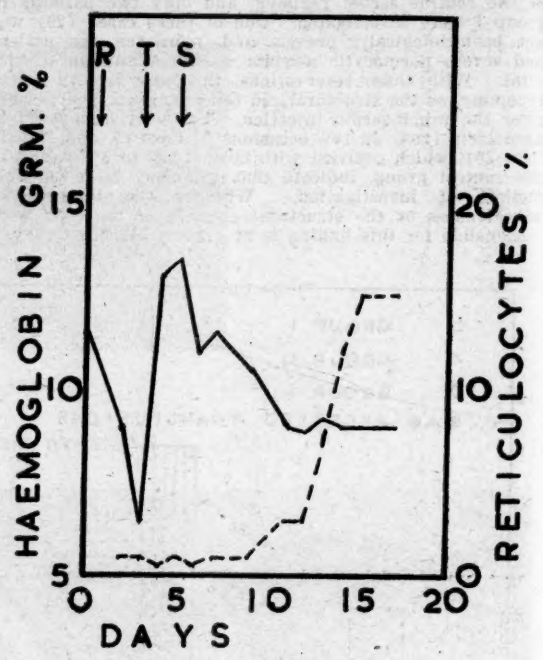

FIGURE VII: Case 6.

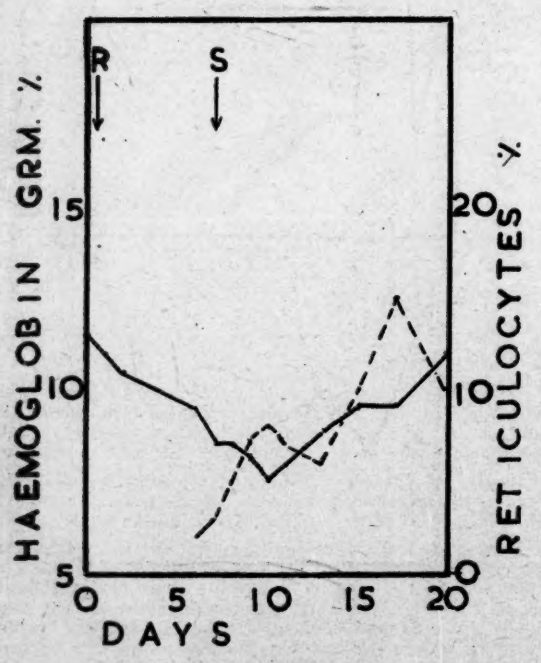

FIGURE VI: Case 5.

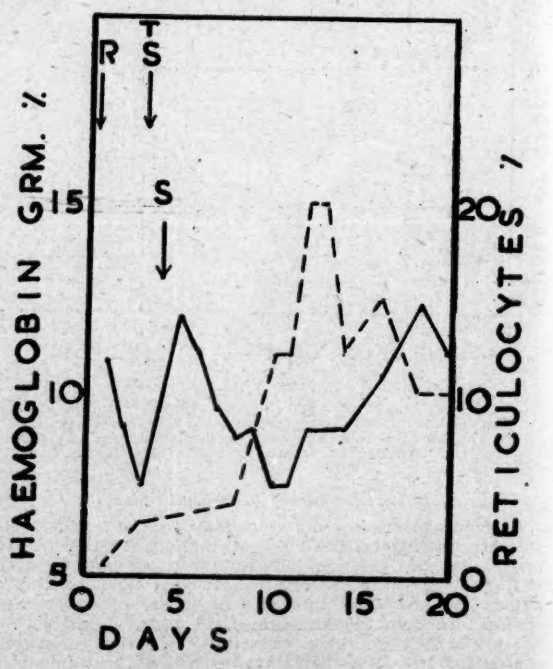

FIGURE VIII: Case 8.

the severity of anæmia in these cases was also not related to the blood group. A detailed analysis of the antigens involved is beyond the scope of this report, but it is suggested that a panagglutinin is chiefly responsible, although the presence of more specific components as well is by no means denied.

Blood Regeneration.

Reticulocyte counts were always very low in the initial days of observation—not an unexpected finding in severe infection. During the second week a sharp rise, often reaching a peak of 20% towards the end of that week, was seen in the cases of group I. This was generally

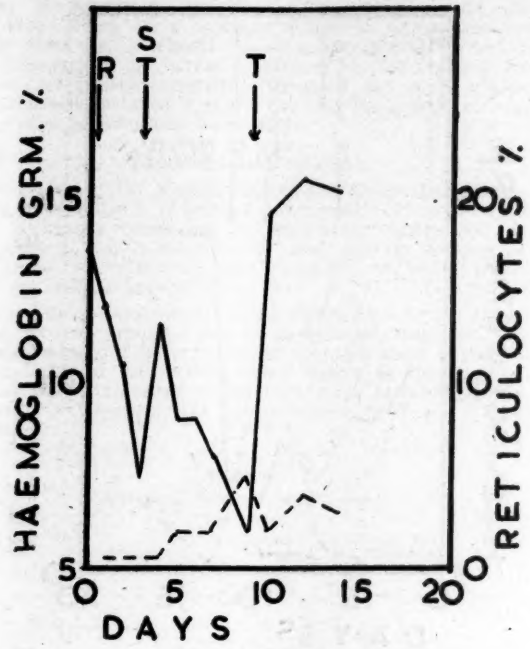

FIGURE IX: Case 9.

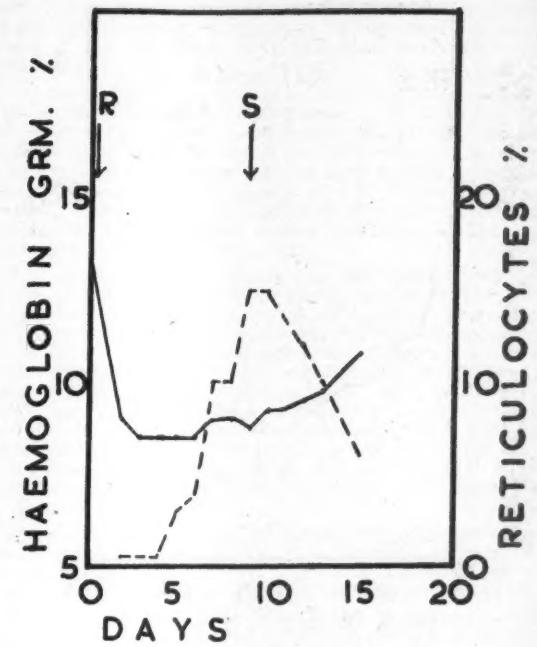

FIGURE XI: Case 11.

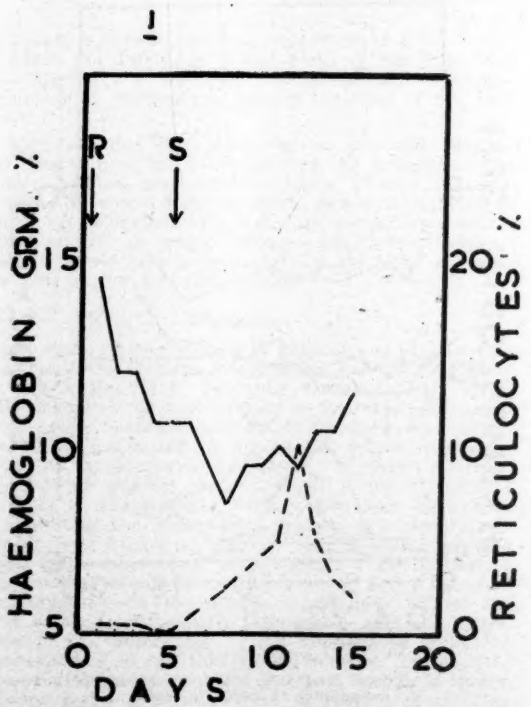

FIGURE X: Case 10.

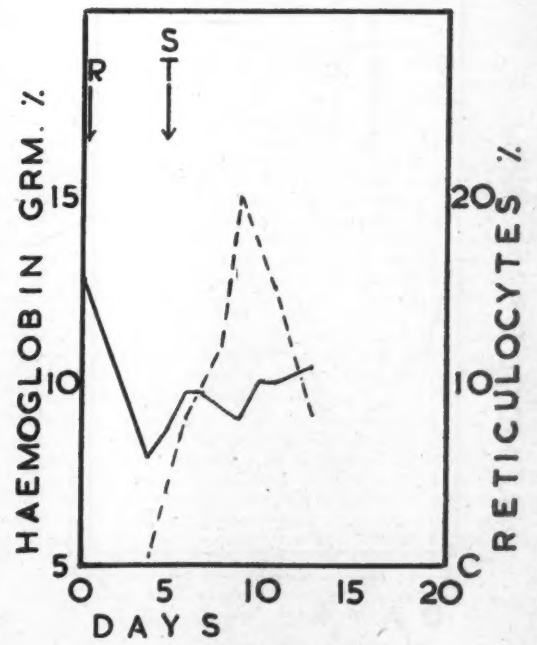

FIGURE XII: Case 12.

proportional to the degree of anæmia, though sometimes masked by a massive blood transfusion. Normoblasts were repeatedly seen in the peripheral blood of the more severely affected children, particularly of the younger age group, and, as in other types of acute hæmolytic anæmia, they appeared in greatest numbers in the early phase of the reticulocyte response. The decline of the reticulocyte curve was more gradual, and in most cases reticulocytes were still increased at the time when the observations were stopped, which was after the hæmoglobin level remained stable or showed a steady rise for some days.

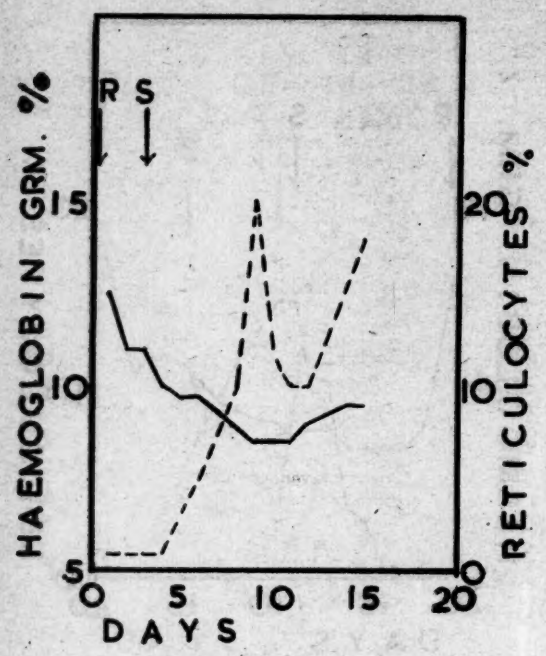

Figure XIII: Case 15.

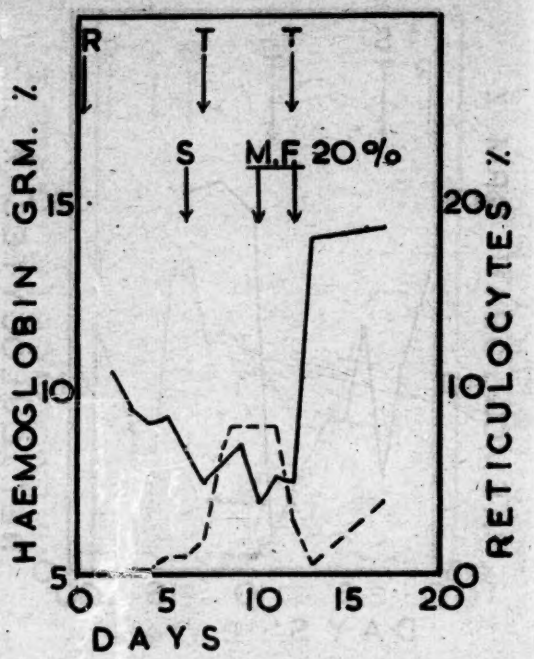

Figure XV: Case 19.

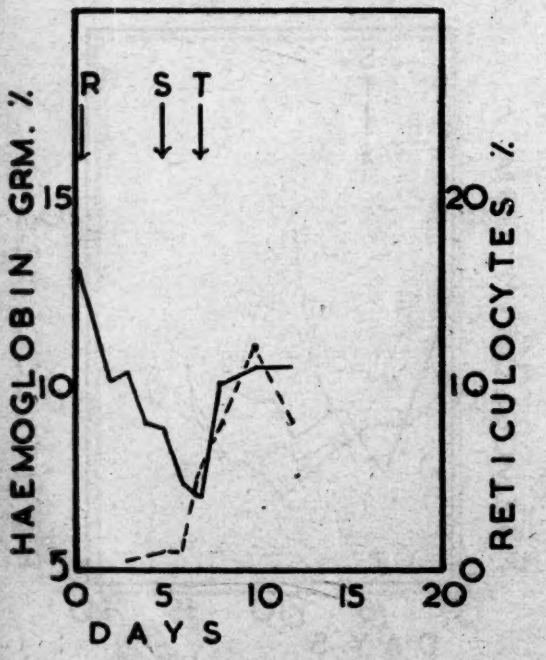

Figure XIV: Case 18.

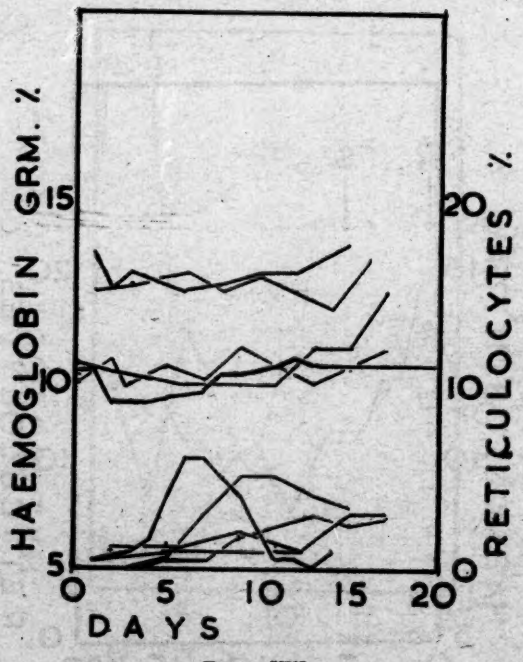

Figure XVI.
Group II (Cases 21 to 25); the lowest set of curves represents reticulocyte levels.

As can be expected, no comparable response could be seen in the other groups (Table I, column 14).

The three patients in group IV deserve separate consideration. They were admitted to hospital long after the time when the routine use of serum had been discontinued, and were given serum for individual reasons. As was shown above, the material used belonged to a new batch, in which the hæmagglutinin content was less than half that found in the previous batches. Furthermore, in Case 46 an infant, aged five weeks, was given only 30 millilitres of serum as compared with the usual 90 to 120 millilitres, and two patients (Cases 45 and 47) were both given transfusions on admission to hospital in anticipa-

tion of hæmolytic anæmia, which, however, did not develop. These cases could be quoted in support of the contention that a critical dose of hæmagglutinating serum is necessary to precipitate hæmolysis, but the group is too small for statistical analysis by itself and could not be legitimately included in any of the previous groups without unproven assumptions being made.

Statistical Considerations.

A glance at the distribution of the lowest hæmoglobin values in groups I, II and III (Figure III) will show that the difference could not be reasonably interpreted as accidental. This is supported by other findings, to mention only the reticulocytosis, the incidence of blood transfusions and the spherocytosis.

Quantitative assessment of the significance of the difference between groups I and II is, however, desirable, not only because the latter is small, but also since it throws some light on the immunological aspect of the anæmia. If the lowest observed hæmoglobin value is taken as the basis of comparison, the values shown in Table II are obtained.

TABLE II.
Hæmoglobin Values in Groups I and II.

Observation.	Group I: Grammes *per Centum.*	Group II: Grammes *per Centum.*
Mean	8·0	10·7
σ	1·598	1·255
Standard error	0·366	0·567

Combined $\sigma = 1{\cdot}541$. With 22 degrees of freedom $t = 3{\cdot}5$, and hence the difference is significant at less than 0·5% level. Similarly, if the total hæmoglobin fall is used, a t value of 3·7 expresses a significance level of the same order.

These estimates are conservative, not only because many figures in group I are likely to be under-estimates, but also because two patients (Cases 13 and 16), who received only small doses of serum, are still included in group I. It is obvious that a similar comparison between groups I and III, or between group I and groups II and III combined, would only greatly increase the level of significance, and is therefore unnecessary.

Discussion.

Other writers have referred to anæmia and the frequent use of blood transfusions in influenzal meningitis (Schiavone and Rubbo, 1953; Beveridge, 1954; Turner, 1948). Turner suspected the rabbit serum as the responsible agent in some cases. Schiavone and Rubbo discuss the possibility of red cell sensitization by a bacterial polysaccharide as a cause of intravascular hæmolysis. In their extensive survey of the clinical records of all types of purulent meningitis at the Royal Children's Hospital, Melbourne, they show that the incidence of anæmia and blood transfusion is much higher in patients with *H. influenzæ* than in those with other types of infection. A comparison of serum-treated and control groups, however, failed to reveal gross differences in the degree of anæmia. Whilst the present series is not strictly comparable with the above, because of the differences in the methods of collecting information and in the time period covered, one possible source of discrepancy could be the fact that even in the Melbourne series a much greater proportion of children treated with serum received blood transfusions, compared with children in the control group (Schiavone and Rubbo, personal communication). This not only points to the difference between these two groups, but also tends to mask the lowest observed hæmoglobin level. If one examines Figure III, it becomes apparent that had the patients been given transfusions at a hæmoglobin level of, say, 9·0 grammes *per centum*, most of the lower figures could not have been recorded. A similar position would arise if the immediate pre-transfusion levels were not estimated.

In the discussion of the actual mechanism of anæmia two components must be distinguished. First, the severity of infection and other predisposing factors such as age and the duration of the illness (Table I) can be correlated with the degree of anæmia existing before serum treatment and that occurring in the control groups. The second component, which is the main aspect of this investigation, is the specific effect of rabbit serum containing human erythrocyte antibodies.

The question of the origin and the exact nature of hæmagglutinins in the rabbit serum can be only briefly discussed. Naturally occurring agglutinins have been demonstrated by many investigators (Hooker and Anderson, 1921; Menolasino and Davidsohn, 1954). Naturally occurring agglutinins are, however, usually present in a much lower titre, and are destroyed by heat. As a counterpart, rabbit red-cell agglutinins are present in normal human plasma and serum (Turner and Jackson, 1943). Severe hæmolytic anæmia and thrombocytopenia have been produced in rabbits by intravenous administration of fresh human serum (Mushett *et alii*, 1953), but the responsible factors are lost on aging.

Intraperitoneal injection of stored human serum containing anti-rabbit agglutinins in a dilution of 1 in 20, in doses of up to 4% of the animal's body weight, failed to produce any demonstrable effects in our laboratory animals.

On the other hand, even small doses of immune antibodies can produce severe hæmolysis in experimental animals. Damashek and Schwartz (1938) produced severe hæmolytic anæmia in guinea-pigs by intramuscular and intraperitoneal injections of small quantities of rabbit serum containing anti-guinea-pig hæmagglutinins and hæmolysins.

Subsequent work has amply demonstrated that the presence of hæmolysins is not necessary, and that immune hæmagglutinins and even plant agglutinins can produce severe hæmolysis *in vivo* (Damashek and Miller, 1943; Castle *et alii*, 1950; Wasatjerna, 1953). Indeed, it is now widely accepted that hæmolysins are not detectable in most clinical hæmolytic syndromes, and that intravascular "sludging" resulting from red cell surface changes can lead to capillary stasis and sequestration, which is followed by a local release of hæmolytic substances by the tissue cells (Knisley *et alii*, 1947; Wasatjerna, 1953). It is significant that the time sequence and the hæmatological changes observed in the present series are almost identical with those described by the authors quoted. The appearance of partial spherocytes, and the much greater changes in mechanical fragility as compared with osmotic fragility, in cases of transfusion reactions resulting from the use of dangerous "universal donors" (Erwin and Young, 1950), also follow the pattern described above.

Although it is probable that the presence of red cell antibodies is sufficient to produce hæmolytic anæmia in any subject and the presence of influenzal meningitis is not a necessary prerequisite, this question can be settled only by direct observation. An opportunity to answer it was lost when a patient, erroneously diagnosed as having *H. influenzæ* meningitis, was given rabbit serum; a pneumococcus was subsequently isolated from the cerebro-spinal fluid. Unfortunately for the purpose of this investigation, the serum given was absorbed with human red cells, anæmia did not develop, and nothing could be proved either way.

Conclusion.

In conclusion it must be stressed that the hæmolytic effect of the specific rabbit serum should be regarded as accidental; the presence of anti-human agglutinins in a high titre probably occurs in some batches of serum only, and may well be the result of some technical detail in its preparation. The absence of anæmia in the three patients treated with the recent batches of serum lends support to this view, and it is quite probable that hæmolytic

anæmia of the type described will not be encountered in future.

Summary.

The occurrence of hæmolytic anæmia in patients with *H. influenzæ* type B meningitis treated with certain batches of specific anti-hæmophilus rabbit serum is described.

Such anæmia did not occur in the control group treated without serum, or with serum absorbed with human erythrocytes, although a varying hæmoglobin deficiency associated with the illness itself was found in some instances.

The view is advanced that the phenomenon is due to hæmagglutinins which were detected in a moderately high titre in the hæmolytic batches of rabbit serum, and it is suggested that these antibodies may have developed accidentally in the animals during the course of preparation of the serum.

The mechanism of hæmolysis is discussed in the light of recent experimental and clinical observations.

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This investigation would not have been possible without the cooperation of the medical and nursing staffs of the Royal Alexandra Hospital for Children.

The photomicrographs were prepared by Mr. J. Sheridan, of the Clinical Photography Department of the Royal Alexandra Hospital for Children.

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Legends to Illustrations.

FIGURE I.—Stained blood film from Case 9 on the ninth day of observation, showing pronounced spherocytosis. The larger cells are polychromatic macrocytes.

FIGURE IIA.—Findings in the same case one day later, after blood transfusion. Note the contrast in appearance of the patient's and the transfused red cells. (Higher magnification.)

FIGURE IIB.—Wet preparation of the cells seen in Figure IIA, showing irregular clumping and bowlshaped red cells.

THE PATHOLOGY OF GOITRE IN TASMANIA.

By ANGUS E. STUART,
Pathology Department, Launceston General Hospital, Tasmania.

GOITRE is endemic in Tasmania and occurs both in the inland regions and in the coastal towns. No studies on the pathology of goitre from this area have yet been reported. The purpose of this paper is to describe the morbid anatomy of thyroid glands from this region and to compare them with those from other goitrous countries.

Material and Methods.

The thyroid glands from 204 consecutive necropsy subjects were weighed and the gross appearance was noted. They were then fixed in 4% formol saline solution and subsequently cut into thin slices, each about one centimetre in thickness, so that the number and type of nodule, if any, might be determined. All glands were examined microscopically.

The following definitions were employed. (i) A normal adult thyroid is one which weighs 15 to 60 grammes, whose substance is uniform and homogenous, and whose follicles are small (approximately 0·25 to 0·5 millimetre in diameter). (ii) A "goitre" is a thyroid which weighs more than 70 grammes. (iii) A nodule or "adenoma" is any circumscribed discrete mass whose naked-eye structure is different from that of surrounding normal thyroid tissue. Only two types are recognized in this communication—namely, the colloid adenoma, which is cystic and succulent, and the parenchymatous adenoma, which is solid in consistency and greyish-white in colour.

Results.

Macroscopic and Microscopic Appearances.

The necropsy thyroid glands are classified in Table I, which shows that approximately 25% of females and 12% of males had multinodular glands. In both the male and female series only 50% of the multinodular glands weighed 70 grammes or over—that is, were of sufficient size to constitute a goitre.

The single nodules were divided into the two groups of parenchymatous nodule and colloid nodule respectively. The incidence and sex distribution of these single nodules are seen in Table II.

The first stage in the development of goitre appears to be the formation of relatively large follicles one to two millimetres in diameter. The gland may or may not be enlarged, and no nodules can be seen on external examination. Fixed glands are homogenous, and the cut surface has a "crystallized fruit" appearance. Histologically the follicles are well filled with colloid, and the bulk of the epithelium is of the low type. The follicles are divided into small nodules one to two centimetres in diameter by fine fibrous tissue septa. Next there is development of obvious nodules clearly visible even on external examination. These nodules are commonly two to three

centimetres in diameter, soft in consistency and well filled with colloid. The follicles are large and frequently show localized areas of hyperplasia—that is, ingrowth of delicate epithelial processes and the presence of columnar epithelium. Figure I shows the ingrowth of hyperplastic epithelium into a macrofollicle, and Figure II shows a more advanced stage of the process. Examination of many sections has frequently revealed transition stages between the colloid adenoma and the solid parenchymatous or so-called fœtal adenoma. It is possible that ingrowth of epithelial processes divides the macrofollicles into smaller follicles, which in turn are divided again. Figure III shows a nodule composed of both microfollicles and larger follicles, and Figure IV shows a uniformly microfollicular structure. It is an interesting possibility that by collapse of microfollicles and absorption of colloid, a solid non-follicular adenoma is formed. Figure V shows the usual histological structure of a non-follicular adenoma.

TABLE I.
Showing Degree of Nodularity of Thyroid Glands.

Classification of Thyroid Glands.	Male Subjects.	Female Subjects.
Normal	80	29
Macrofollicular with internal nodularity ..	9	5
Single nodules	17	13
Two or three nodules	11	7
Multinodular	15	18
Total	132	72

Histological Findings in Single Nodules.

The colloid type of nodule contained large follicles filled with colloid and lined by flattened or cuboidal epithelium. The nodules were surrounded by compressed thyroid parenchyma and were partially or wholly encapsulated by fibrous tissue of varying thickness.

The parenchymatous type of nodule varied in size from 0·5 to 3·0 centimetres in diameter, was greyish-white in colour, contained little colloid and was usually well encapsulated. These nodules were invariably microfollicular in structure and frequently showed central degeneration. In hæmatoxylin and eosin stained preparations the latter took the form of isolated and atrophic follicles separated by large amounts of structureless eosinophilic material. In sections stained with Gallego's method this degenerate matrix retained the blue colour, as did the colloid in the atrophic follicles, whereas the colloid in normal follicles stained bright yellow.

Discussion on Necropsy Specimens.

Comparison with Swiss and American Goitres.

In America the goitre zone is found around the Great Lakes and Saint Lawrence valley, extending westward through Minnesota, the Dakotas and adjacent Canadian territory. Goitre is, of course, still endemic in Switzerland and appears to be more severe in the north-east Cantons. In both these countries, as in Tasmania, the common form of goitre is the nodular variety, and it occurs with greatest frequency in patients over the age of thirty years. From a strictly pathological and histological point of view, there appears to be no difference in goitre specimens from Tasmania, America and Switzerland.

Incidence of Single Nodules.

The incidence of single nodules in our series appears high (15%), a point in disagreement with Joll's statement that single adenomata are apparently rare in endemic areas.

Single nodules are of particular interest as regards their alleged frequent association with carcinoma. Cope (1947) found that cancer occurred in 19% of thyroid glands which contained single nodules. His figures were taken over a twelve-year period at the Massachusetts General Hospital. Boyd (1937) in England found only 78 single nodules in a series of 843 goitres. He stated that they did not recur on removal and were innocent neoplasms. Comparison of series of cases of nodular goitre purporting to show a relationship to malignant disease is notoriously misleading. Factors of selection, together with variable criteria for the histological diagnosis of carcinoma, render interpretation difficult. None of the single nodules described in the Tasmania necropsy series showed signs of malignant change.

The Relationship of Goitre to Iodine Deficiency.

Goitre may be caused by an absolute deficiency of iodine in the environment, or by other factors which render iodine unavailable to the host, either by combining with iodine outside the body or by preventing its utilization in the thyroid gland itself. Thus it is possible that the iodine of foodstuffs may thereby be diverted from proper usage by the nature of the diet. St. Lager (1867) stated that ingestion of foods rich in fats, particularly pork, was an important factor in the causation of goitre. McCarrison (1919) showed that diets which include an excessive amount of digestible fats are potent in causing thyroid hyperplasia. He also made the interesting observation that a mild degree of thyroid hyperplasia occurred in pigeons fed on a diet rich in onions. At that time he did not have access to chemical analysis of his "oil of garlic", and the importance of the sulphydryl group in the thyroid gland metabolism was not realized until some years later. Marine and Lenhart (1930) demonstrated that pig's liver was the most potent of a variety of meats in causing goitre in dogs. Greenwald (1950) states that feeding of iodine-deficient diets has never produced goitre in animals, and in a provocative article casts considerable doubt on the iodine-lack hypothesis.

In certain areas in Tasmania goitre is still prevalent despite iodine prophylaxis, and on occasion one may see a goitre continue to enlarge despite continued and adequate provision of iodized salt. I believe that in Tasmania iodine has for too long been the central figure in the study of goitre, and that those naturally occurring factors which will prevent either absorption or utilization of iodine are in need of closer examination.

TABLE II.
Type and Sex Incidence of Simple Nodules.

Types of Single Nodule.	Male Subjects.	Female Subjects.
Parenchymatous ..	10	10
Colloid	7	3

Summary.

The thyroid glands were examined from 204 consecutive necropsy subjects in a region of endemic goitre. Approximately 25% of females and 12% of males had multinodular glands.

Some of the difficulties in accepting the iodine-lack hypothesis in regard to the ætiology of goitre in this area are discussed. It is suggested that further investigation into naturally occurring goitrogenic agents in Tasmania is required.

Acknowledgements.

I wish to thank Dr. J. L. Grove and Dr. A. Pryde for help and advice in the preparation of this paper, and also Dr. W. Taylor and Dr. H. E. Hutchison for valuable assistance with the manuscript.

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Legends to Illustrations.

FIGURE I.—Ingrowth of hyperplastic epithelium into a follicle.

FIGURE II.—Formation of small follicles within a macrofollicle.

FIGURE III.—Macrofollicular and microfollicular structure.

FIGURE IV.—Uniformly microfollicular structure.

FIGURE V.—Non-follicular adenoma.

Reports of Cases.

RUPTURE OF SPLENIC ARTERY ANEURYSM IN PREGNANCY.

By L. O. S. POIDEVIN,
Adelaide.

THE rarity of rupture of a splenic artery aneurysm in pregnancy is sufficient justification for the reporting of a recent case. The literature was reviewed by Lennie and Sheehan in 1942 and by Chalmers in 1949, and a complete revision is not intended here.

The actual number of cases reported is somewhat vague. Lennie and Sheehan reported 16 in their review, and in a note at the end of their paper mentioned four more which appeared whilst their article was in publication. Other authors reporting one each since then have been Danforth (1945), Chalmers (1949) and Tennant and Starrit (1950). As my search of the literature has not been conclusive, I can only suggest that probably less than 30 cases have been reported including the present case. Of all these only two patients appear to have survived rupture of such an aneurysm during pregnancy; one case was reported by Gillam (1942) after a splenectomy and a subsequent laparotomy for an abscess; the other was reported by MacLeod (1940), whose case was actually one of ruptured splenic artery with no evidence of an aneurysm.

The overall autopsy incidence of splenic artery aneurysms as given by Lennie and Sheehan is 0·05%, whereas all types of aneurysms have an incidence of 1·26%. Aneurysms of the splenic artery occur three times as frequently in females as in males, and there is a higher incidence amongst pregnant females than among the non-pregnant. The reason for this is not known; but because almost all the cases have occurred in late pregnancy I suggest that the increasing abdominal enlargement is a factor.

The ætiology of aneurysms of the splenic artery is possibly congenital weakness involving a failure of the media (Figure I), and particularly could this apply at bifurcations. Vascular disease as a cause in the younger group is unlikely.

Clinical Record.

Mrs. A., aged twenty-four years, was pregnant for the sixth time. Her last menstrual period had occurred on August 29, 1953, and she was booked in my clinic at the Queen Victoria Maternity Hospital, Adelaide. Although this was the sixth pregnancy, there was only one living child. The first-born died when two weeks old with a respiratory infection. The second and third pregnancies terminated in miscarriages, the fourth in a still-born premature baby, and the fifth in a living child weighing nine pounds 14 ounces at birth.

This sixth pregnancy had been uneventful until May 6, when the patient began complaining of "indigestion" pains. Between May 6 and 16 she complained on three occasions of sudden sharp pains in the epigastrium, each attack being nocturnal and waking her and causing her to sit up and gasp for breath. The duration of the attacks was so short that medical aid was not called. On May 16 she went for a picnic and was in good form, but whilst washing up some dishes at 7 p.m. she was suddenly seized with severe pains in the epigastrium, and breathing was so difficult that she went outside to get her breath and then collapsed.

On her admission to the Queen Victoria Maternity Hospital at 11.40 p.m. she was comatose with extreme skin pallor; cyanosis of the finger tips, air-hunger, restlessness and retching were apparent. Her pulse rate was 140 per minute and the pulse was of poor volume; her blood pressure was 90 millimetres of mercury, systolic, and 60 millimetres, diastolic. Her abdomen was soft and tender, although it had been reported by an earlier observer as rigid; the uterus was easily defined with its fundus two fingers' breadth below the costal margin. The fœtus was palpable; it was lying longitudinally with the presenting vertex engaging the brim. No fœtal heart sounds were heard. Dulness was apparent in both flanks and the epigastrium. There was no vaginal bleeding, and digital examination confirmed the head presentation and a "ripe" cervix.

Resuscitative measures included intraarterial blood transfusion as well as the intravenous administration of blood and serum, together with oxygen given by the intranasal route, and the keeping of the patient warm.

By 1 a.m. on May 17 her colour had improved, particularly after the intraarterial transfusion. At the same time it was apparent that the abdomen was more distended with fluid, that some major arterial rupture was responsible, and that her survival depended upon controlling this vessel, which from the history was in the upper part of the abdomen. A laparotomy was performed through a left paraumbilical incision under anæsthesia with a maximum amount of oxygen and a minimum amount of nitrous oxide.

Many pints of fresh and old blood escaped from the wound whilst an examination of the uterus was made. This was intact and soft, and when the wound was enlarged upwards the trouble centre was located in the lesser sac. To facilitate a further search the uterus was emptied through a classical incision and a still-born male fœtus was delivered. No hæmorrhage occurred from the uterus, and after being sutured it remained quite flabby. The lesser sac was felt to be filled with blood clot, and fresh blood came freely through the foramen of Winslow; examination of the gastric wall revealed extensive induration with hæmorrhage. The patient's condition justified no further surgical procedure, so the abdominal wall was closed with the thought of a rupture of the splenic artery as the most likely diagnosis. Respirations ceased during the closure. The operation occupied fifteen minutes.

At autopsy nine hours later the lesser sac was opened and found to contain masses of old organizing blood clot. The pancreas was indurated with clot, and a ruptured aneurysm was found on the middle section of the splenic artery (Figure II).

Discussion.

The history was unusual and immediately gave warning of some extraordinary happening. On looking back, having seen the infiltration of organized blood in the pancreas, I am sure that this girl had a slow leak from the aneurysmal sac during the preceding few days. This was the first stage of the rupture. It is interesting that this slow leakage of blood into the lesser sac and pancreas caused epigastric pain and gasping for breath. Interesting also is the short duration of these episodes, and the fact that in between them she felt quite well and even went out for a whole day's picnic on the day of the final rupture.

This history should be remembered, for one day these unusual symptoms will be met again, and it may help others in making an earlier diagnosis than was possible in this case.

It is unlikely that the maternal mortality from rupture of a splenic artery aneurysm will be reduced unless the diagnosis can be made during the first stage of rupture. In most cases reported the patients have given a history of the two stages of rupture with varying intervals between the two episodes. Once the second stage or final rupture eventuates, overwhelming hæmorrhage occurs into the lesser sac and via the foramen of Winslow to the greater sac, and to rescue a pregnant patient at this stage must mean heroic surgery involving laparotomy on a seriously shocked patient, Cæsarean section and either splenectomy or ligation of the splenic artery proximal to the rupture, the spleen being left in the hope that aseptic atrophy will occur.

The diagnosis after the first or leaking stage will not be easy. It is not likely to be thought of, which is all the more reason for remembering the possibility. The history,

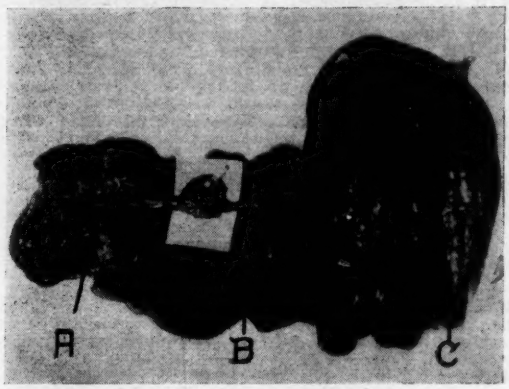

FIGURE II.

Showing the aneurysm of the splenic artery with hæmorrhagic infiltration of the pancreas. A, aorta; B, pancreas infiltrated with blood; C, spleen.

therefore, would probably be the most important hurdle in diagnosis. Auscultation over the left hypochondrium may reveal an odd murmur. Arteriography may give a positive diagnosis. If this syndrome is suspected, laparotomy should be undertaken before the final rupture occurs.

Acknowledgement.

My thanks are due to Dr. Dudley Parker, of the Department of Anatomy, University of Adelaide, for his help in performing the autopsy and preparing the sections.

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Legend to Illustration.

FIGURE I.—On the right the muscle layer (kinked) of the splenic artery is illustrated, and on the left of the aneurysmal wall. The "fade-out" of the muscle layer is well shown.

Reviews.

The Year Book of Drug Therapy (1954-1955 Year Book Series), edited by Harry Beckman, M.D.; 1955. Chicago: The Year Book Publishers, Incorporated. 8″ × 5¼″, pp. 592, with 74 illustrations. Price: $6.00.

THIS is an admirable volume, and few members of the Year Book Series will have such a wide appeal. Its topical importance is made obvious by the long list of significant developments in drug therapy during the year covered which are set out in an introduction by the editor, Harry Beckman. The many abstracts, drawn from a wide range of journals, are arranged conventionally. Two opening chapters deal with allergy and with antibiotics and sulphonamides. A long chapter on cardio-vascular diseases is subdivided into sections on arrhythmias, congestive heart failure, coronary disease, endocarditis, hemiplegia, hypertension, peripheral vascular diseases, and thrombosis (other than coronary), thrombophlebitis and the anticoagulant drugs. Then follow chapters on the main subdivisions of medicine (dermatology, endocrinology *et cetera*); the chapter on internal medicine deals particularly with infectious diseases, kidney disturbances, liver and gall-bladder disorders, neoplastic diseases, obesity, chest diseases, *diabetes mellitus*, pain, poisoning, rheumatic disorders, sprue, thyrotoxicosis, and worms and flukes. The editorial comments are brief, sane and refreshing.

Ciba Foundation Symposium on Chemistry and Biology of Pteridines, edited by G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch., and Margaret P. Cameron, M.A., A.B.L.S.; 1954. London: J. and A. Churchill, Limited. 8¼″ × 5½″, pp. 440, with 143 illustrations. Price: 42s.

THE latest Ciba Foundation symposium in the general series deals with the chemistry and biology of the pteridines. From March 22 to 26, 1954, twenty-nine authorities on various aspects of the subject from Europe and North America met in London and papers were read and discussions held.

Sixteen papers, each with discussion, on the purely chemical aspects of the pteridines were given. These papers are of high quality but will be of interest only to chemists working in the highly specialized field of the pteridines and related fields.

The second half of the work has twelve papers with discussions on the biological aspects of the pteridines. Most of the papers here, while containing important data on the effects of pteridines such as folic acid and folic acid analogues on cell metabolism, will have a rather narrow appeal among biologists and physicians. Four papers which contain much that will interest medical men are "The Yellow Pigment of the Argentaffine Cells of the Mammalian Intestinal Tract" by W. Jacobson, "Some Aspects of Disordered Folic Acid Metabolism in Man", by R. H. Girdwood, "Occurrence of Hepatic Fibrosis in Children with Acute Leukæmia Treated with Folic Acid Antagonists" by J. Colsky, and "The Mode of Action of Folic Acid Antagonists and the Function of the Leuconostic Citrovorum Factor" by W. Jacobson. The discussions right through are particularly good and the whole book follows the very high standard set by its predecessors.

The Lipids: Their Chemistry and Biochemistry. By Harry J. Deuel, junior; 1955. New York: Interscience Publishers, Incorporated. London: Interscience Publishers, Limited. In three volumes. Volume 2: "Biochemistry: Digestion, Absorption, Transport and Storage." 9½″ × 6¼″, pp. 936, with 33 text figures. Price: $25.00.

VOLUME I of this work by Harry J. Deuel, junior, dealing with the chemistry of the fatty acids and their derivatives, and the carotenoids, sterols and fat-soluble vitamins appeared a few months ago. Volume II dealing with certain aspects of the biochemistry of the lipids has now appeared. This volume treats of digestion, absorption, transport and storage. It is a monumental work; this volume has over 900 pages of text. The author seems to have read every paper of importance published on these aspects of the lipids; there are 630 references and 48 pages of names of authors consulted. Several tests failed to show important work missed. In the 345 pages dealing with digestion, absorption and digestibility of fats and other lipids every aspect has been considered in detail. Where there are differences of opinion between different observers the cases are presented fully and fairly. Thus the partition theory of Frazer of fat absorption from the animal intestine is given very fully and contrasted with the older theories. One infers that the author favours the Frazer theory, but this is not stressed.

One hundred and seventy-two pages are given to discussion on the blood lipids, 186 pages to the occurrence of lipids in the animal as a whole and 110 pages to the lipid distribution in specific tissues and in their secretions. The considerable detail given to the chemistry and properties of the bile salts and derivatives of them seems rather out of place, as the information can easily be obtained elsewhere. Although the term lipids includes cholesterol and other sterols, carotenoids and the fat-soluble vitamins, as well as fats and fatty acids, phospholipids and allied compounds, one wonders if the non-fatty acid compounds could not better have been considered in a separate volume.

This book is an authoritative account of those aspects of the lipids considered and must long remain as a very valuable reference book. The presentation is clear and readable, if a little diffuse at times. It is a "must" for organic chemistry and biochemistry libraries.

Notes on Books, Current Journals and New Appliances.

Goodbye Harley Street. By R. Scott Stevenson; 1954. London: Christopher Johnson. 8¼" x 5¼", pp. 224. Price: 15s.

DR. R. SCOTT STEVENSON has had an interesting life—his book, "Goodbye Harley Street", bears witness to this. His reminiscences make good reading. He became known to Australian medical officers in the north of France during the 1914-1918 war, where he took a part in the concert parties that helped to brighten the lives of patients at base hospitals, and incidentally of their staffs. He had had some experience of writing and after the war was over joined for a period the staff of the *British Medical Journal* when the late Sir Dawson Williams was editor. His comments on the journal and those who were responsible for its production are illuminating. Through the "inspiration and energy" of Dr. Hugh Clegg the *British Medical Journal* has become "the most important medical publishing house in the country". Dr. Stevenson discusses the advent of the National Health Service to Great Britain in a way that one would expect from his affiliations. He takes his readers to Paris and America, and ends his book with two chapters on deafness. This book is carefully and attractively written. When he puts it down the reader will understand the author's contentment with his new house at Gibraltar, where he practises his specialty of oto-rhino-laryngology, which appears to be the true love of his life.

British Medical Bulletin.

UNTIL a few years ago the known facts about the coagulation of the blood could be set out in a comparatively simple way. Recently, research on the subject has been greatly accelerated and blood coagulation is now seen to be a very complex process or rather series of processes. Volume XI, Number 1, 1955, of the *British Medical Bulletin* is wholly taken up by papers on blood coagulation and thrombosis and the practical application of the new knowledge in medicine. A brief introduction is given by R. G. Macfarlane. R. Biggs deals with the "Assessment of Clotting Efficiency" and discusses the various tests of clotting function. W. R. Pitney and J. V. Dacie treat of "Hæmophilia and Allied Disorders of Blood Coagulation". The various kinds of hæmophilia are considered and the diagnosis and treatment for each are discussed. C. Hougie deals with "Circulating Anticoagulants", substances in the blood of certain types of patients which prevent the formation of blood thromoplastin. J. F. Ackroyd has two articles, one on the "Role of Platelets in Coagulation, Thrombosis and Hæmostasis, with Some Observations on Platelet Dysfunction, including Thrombasthenia", and the other on "Platelet Agglutinins and Lysins in the Pathogenesis of Thrombocytopenic Purpura, with a Note on Platelet Groups". The titles show the subjects of the articles. J. B. Duguid has a very interesting discussion on "Mural Thrombosis in Arteries". He indicates the frequency of this condition and its relation to atherosclerosis and atheroma. A. S. Douglas considers "Mode of Action of Coumarin Drugs" and C. C. Burt "Clinical Application of Anticoagulant Drugs", while R. B. Hunter and D. M. Shepherd give the "Chemistry of Coumarin Anticoagulant Drugs". In "Nature of the Fibrinogen-Thrombin Reaction" K. Bailey and F. R. Bettelheim set out in detail the modern views on the mechanism of blood clotting. The "Chemistry and Mode of Action of Heparin and Related Compounds" is dealt with by K. W. Walton. From the titles of the articles it will be clear that the subject of blood coagulation has been covered very fully and as all the writers are outstanding workers in the field the whole publication is of a very high standard. All who are interested in blood coagulation and thrombosis should study it.

A Therapeutic Index: A Guide for Housemen and Practitioners, by C. M. Miller, M.D. (London), M.R.C.P. (London), and B. K. Ellenbogen, M.D. (Liverpool), M.R.C.P. (London), with a foreword by E. Noble Chamberlain, M.D., M.Sc., F.R.C.P.; 1955. London: Baillière, Tindall and Cox. 7½" x 5", pp. 160. Price: 12s. 6d.

THE treatment described in this book is orthodox enough and up to date, but its value is limited by its brevity. This is slightly paradoxical, as the authors' aim is above all to be brief. This makes for ease of reference and keeps the book small enough to be slipped into a resident medical officer's pocket or a practitioner's bag, and it is made clear that there is no intention of supplanting the larger textbooks on treatment. Nevertheless, it is debatable whether, for any purpose, an adequate description of treatment is possible in the number of words used—for example, 100 for leuchæmia (acute and chronic), 150 for malaria, 240 for rheumatic fever, 70 for botulism, 60 for disseminated sclerosis. As an *aide mémoire* for practitioners it should be acceptable, but the young resident medical officer will be wise to seek more detail elsewhere.

Modern Treatment Year Book, 1955: A Year Book of Diagnosis and Treatment for the General Practitioner, edited by Cecil Wakeley, K.B.E., C.B., LL.D., M.Ch., D.Sc., F.R.C.S., F.R.S.E., F.R.S.A., F.A.C.S., F.R.A.C.S.; Twenty-First Edition; 1955. London: Published for the Medical Press by Baillière, Tindall and Cox, Limited. 9" x 6", pp. 370, with 45 illustrations. Price: 25s.

A valuable feature of the 1955 edition of this hardy annual is the series of nine articles on antibiotics; these deal with their roles in medicine, surgery, neurology, skin diseases, tuberculosis, venereal diseases, ophthalmology and urinary infections and with the emergence of antibiotic-resistant strains of bacteria. The remaining 27 articles, all by men of eminence in their own fields, range over a wide number of subjects including the new insulins, infections of the hand, intractable pain, "growing pains", depressive states and prolonged labour. The high standard of these yearly volumes is well maintained.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Surgery of the Heart", by Charles P. Bailey, M.D., M.Sc. (Med.), LL.D. (Hon.), F.A.C.S., F.C.C.P., F.I.C.S.; 1955, Philadelphia: Lea and Febiger. Sydney: Angus and Robertson, Limited. 9½" x 6½", pp. 1062, with 1455 illustrations, three in colour. Price: £13 8s. 9d.

The author aims to present certain concepts and techniques which have been proven sound, to stimulate undergraduate and graduate students who may some day become cardiologists, and to acquaint practising doctors with the concepts, indications for surgery and so on.

"Peripheral Vascular Diseases", by Edgar V. Allen, B.S. M.A., M.D., M.S. in Medicine, F.A.C.P., Nelson W. Barker, B.A., M.D., M.S. in Medicine, F.A.C.P., and Edgar A. Hines, junior, B.S., M.A., M.D., M.S. in Medicine, F.A.C.P., with associates in the Mayo Clinic and Mayo Foundation; Second Edition; 1955. Philadelphia: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical), Limited. 9½" x 6½", pp. 838, with 316 illustrations, seven in colour. Price: £6 3s. 6d.

There are 27 chapters in the compilation of which the three authors have been assisted by 13 contributors.

"Clinical Diagnosis", by Elmer G. Wakefield, B.S.A., B.Sc., M.D., F.A.C.P.; 1955. New York: Appleton-Century-Crofts, Incorporated. 10" x 6½", pp. 1618, with 21 text figures. Price: $22.50.

Planned to cover the common as well as the uncommon diseases and divided into three parts: "Regional Diagnosis", "The Systemic Diseases", "The Body as a Whole".

The Medical Journal of Australia

SATURDAY, JUNE 18, 1955.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words of phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

A MEDICAL SCHOOL FOR WESTERN AUSTRALIA.

IN the issue of June 26, 1954, the establishment of a medical school for Western Australia was discussed. It was explained that the establishment of a medical school in Perth was by no means a new subject for the columns of this journal. Readers of this journal must by now be well aware of the pertinacity with which the establishment of such a medical school has been advocated during recent years. They will remember that in July, 1946, Professor Peter MacCallum, who was then Dean of the Faculty of Medicine in the University of Melbourne, was invited by the Premier of Western Australia to visit that State in order to collect the evidence necessary to the project and to give the Government the benefit of his advice. This is evidence—if indeed such evidence is required—that the Government of Western Australia has taken the matter seriously for some time. In our advocacy last year, we discussed it from several points of view and concluded that a school founded in faith and hope, with firmness of will and complete understanding, would live and grow and benefit those amongst whom it was placed as well as those who were numbered among its offspring. On June 26, 1954, we also published a special article by Dr. Eric G. Saint, the Director of Clinical Research at the Royal Perth Hospital. Here Dr. Saint drew attention to the fact, also mentioned in the leading article in that issue, that the decision of the University of Adelaide not to accept any more Western Australian students for teaching in the clinical years after 1956 had given special urgency to the problem. Dr. Saint concluded that the argument was unanswerable—that population expansion, economics, the crisis in medical education, and internal pressures within the State itself, made the establishment of a medical school in Western Australia more than merely desirable: they made it an urgent necessity. He stated that capital cost was the bogy which scared legislators and that they should derive assurance from the fact that there were those who believed that the ideal of a university was of greater worth than bricks and mortar, that the problem of adapting local buildings and hospitals was not insuperable, and that costs need not be astronomical.

Early in the present year the Premier of Western Australia gave further evidence of the Government's sincerity in the matter, for on January 28 he set up a special committee to advise the Government on the proposed medical school and to investigate the estimated costs and stages of the building programme together with the staffing of the school and organization of the courses. The members of the committee were as follows: Mr. H. W. Byfield (Under-Treasurer), Dr. Leslie Henzell (the Commissioner for Public Health), Mr. J. Griffiths (Administrator of the Royal Perth Hospital), Mr. S. L. Prescott (Vice-Chancellor of the University of Western Australia), Dr. E. G. Saint (Director of Clinical Research at the Royal Perth Hospital), and Dr. J. P. Ainslie (representing the Western Australian Branch of the British Medical Association). The committee took as the basis for its study the preliminary submission made to the Premier by the Senate of the University of Western Australia in June, 1954. It interviewed the executive officers and boards of management of the four leading hospitals in and around Perth and also a number of persons representing university, departmental and other bodies. The findings of the committee are set out in six paragraphs, the substance of which is as follows:

1. A medical school designed to meet the needs of Western Australia can be established as a faculty of the University of Western Australia, and reasonably adequate accommodation can be made available to meet the requirements of the State for up to fifteen to twenty years. The committee is convinced that the establishment of such a medical school is a necessity.

2. It would cost £278,046 to establish the medical school. This amount was made up of £184,057 for the pre-clinical school at the Crawley site, and £93,989 for the clinical department established in conjunction with declared teaching hospitals, namely, the Royal Perth Hospital, the King Edward Memorial Hospital for Women, the Princess Margaret Hospital for Children and the Fremantle Hospital. The committee pointed out that these estimates would vary in the event of any marked economic change in Western Australia.

3. At the present economic level, the annual running costs would not exceed £94,716, made up of £38,955 for the pre-clinical departments of anatomy, physiology and biochemistry, and £55,761 for the clinical departments of pathology, bacteriology, medicine, surgery, obstetrics and gynæcology, child health and the various specialties. The committee added that staffing costs would naturally need to vary in accordance with salary variations that might take place in other universities within the period under review.

4. The committee strongly recommends the setting up of a complete school with training in all years of the medical course. It recommends that the clinical teaching should commence in 1957 for Western Australian students who have completed their pre-clinical course at the University of Adelaide, and that pre-clinical training in Western Australia should start in 1958. To enable this to take place, governmental decision would have to be made not later than the end of April, 1955, so that the necessary appointments could be made and building adaptations commenced.

5. The committee's main conclusions are elaborated in addenda to the report. In the first place, there is a general description of the problem and the method recommended for solution (this occupies three separate parts). Secondly, details of accommodation planning and estimates are given in two separate parts. Thirdly, consideration is given to the necessity for special legislation in one part. Recommendations for the starting date of the school are discussed in another part, and the last part deals with the question of fees.

6. The committee states that in the performance of its task it has become very concerned with medical and hospital problems which will face the State during the next twenty years. The increasing shortage of hospital beds in the metropolitan area and the recommendations already made to the Government by the State Health Council to make good these shortages progressively will have an important influence on the planning of medical education in the future. The committee thinks that it would be failing in its duty if it did not draw to the Government's attention the seriousness of the situation. It has included a special addendum dealing with the matter.

The main body of the report is set out in the addenda or parts which have been described. For the information of readers, only the main portions will be considered. In Part I the committee has submitted a general survey of the proposals and of the reasons which have prompted it to make its several recommendations. In the description of "a medical school" it is stated that there are good, bad and indifferent medical schools throughout the English-speaking world, to be distinguished from each other not so much by the material consideration of bricks and mortar, but by the palpable spirit which enlivens some and is lacking in others. This is what our nonagenarian medical philosopher, Dr. Robert Scot Skirving, of Sydney, in speaking of a hospital, describes as its "soul". The committee insists that pride demands that when a medical school in Western Australia does come into being, it shall receive international acclaim. The committee therefore has, to quote its words, "had to give a great deal of thought to this immeasurable quality—the spirit of a medical school". Good medical schools are recognized by the excellent qualities of their graduates, in whom certain moral and intellectual characteristics are clearly discernable. The "good doctor" is "well-informed, and studiously strives to keep himself well-informed throughout his life; his responsibilities to his patients and to the society he serves outweigh self-interest—that is to say, he is motivated by a strong sense of duty; his clarity of thought makes him widely respected, not only among those able to judge his clinical capacities, but in the world of public affairs; his integrity is a shining example to others". A good medical school thus imparts not only factual knowledge to its students but also a love of knowledge for its own sake; it also engenders the spirit of moral purpose and develops a social conscience, and it demonstrates an ideal of integrity of thought and conduct. To this end there must be integration of the student's study and a body of teachers with a unity of purpose. Through a medical school the community may expect to benefit more directly by an overall improvement in the standards of medical practice. The community is, of course, benefited incidentally by research conducted within the walls of the university. The direct benefits to the community will arise because teachers in the several subjects will improve the standards of work that is carried out as a result of their studies. "The exact standards of diagnosis and treatment imposed by the self-discipline of teaching will improve patient-care throughout the State."

In discussing the site of the new medical school, the committee makes observations which will be heartily commended by most people. It holds that to build a new, complete medical school with a related teaching hospital would be a formidably expensive undertaking and would delay the commencement of medical teaching for many years to come. In its opinion, it is very doubtful if the best way to start a medical school is to begin in new, lavishly equipped buildings. The University of Western Australia has "grown from simple and humble beginnings". We recall that the Medical School of the University of Sydney was started by the late Thomas Peter Anderson-Stuart in a four-roomed cottage. The committee recommends that use should be made of existing buildings. It thinks that the pre-clinical school should be housed mainly in hutments at Crawley, next to the Institute of Agriculture, and that the clinical school should be based at the Royal Perth Hospital. The pre-clinical school would comprise a school of anatomy in one remodelled hut, a school of physiology in another, and a newly built school of biochemistry with the necessary students' and locker rooms. The proximity of these three departments to one another is desirable from every point of view. "The integration of anatomy and physiology and biochemistry in student teaching is one of the more difficult problems of medical education, and it is hoped that Western Australia might make a significant contribution to method in this field." In regard to teaching hospitals, the committee has considered those which have both in-patient and out-patient departments, casualty services, large proportions of "public" beds, resident medical and honorary medical staffs and well-equipped ancillary services. The four hospitals which fulfil these requirements are the Royal Perth Hospital, the Fremantle Hospital, the Princess Margaret Hospital for Children and the King Edward Memorial Hospital. The Royal Perth Hospital will provide the bulk of clinical experience; most of the students' time will be spent there, and it is logical that the clinical school with all its departments, common rooms, lecture theatres and administrative offices should be based there. The interesting suggestion is made that senior clinical students would profit considerably by a short period of residence at the Fremantle Hospital in their final year, and its board has promised to find accommodation for four to six students-in-residence.

The problem of staff is complicated by the fact that few medical graduates in Western Australia have previously held university teaching appointments and few have had any previous undergraduate teaching experience. The committee recommends that chairs of anatomy and of physiology and biochemistry be set up with appropriate staffs of lecturers and technicians. It is also recommended that part-time demonstratorships should be offered in these subjects. In discussing the subjects of pathology and bacteriology (microbiology), the committee states that the Public Health Department is anxious to expand its microbiological services as part of its responsibility in the control of infectious and epidemic diseases of the States. The committee recommends the appointment of a professor of pathology with a senior lecturer and a lecturer, and a reader in microbiology with a lecturer. It is thought that this arrangement will answer Western Australia's special needs. The professor of pathology would organize undergraduate and post-graduate teaching and would also act as consulting pathologist to the Royal Perth Hospital, being in charge of its department of pathology; his assistants would be responsible for the routine diagnostic work of the hospital. In microbiology, the reader would organize undergraduate teaching and would, with the aid of a lecturer, organize the routine diagnostic work of the

hospital. In addition, he would also act as director of bacteriology in the Department of Public Health. In regard to the clinical subjects of medicine, surgery, child health and obstetrics and gynæcology, the committee is opposed to the appointment of part-time consultants to teach these specialties, for the following reasons: (i) There are few local men in Western Australia who have matured as practising specialists in a medical school environment, with teaching experience as juniors, as in other States. (ii) There are few local men willing to sacrifice a great proportion of their private commitments to undertake the onerous task of organizing teaching in the initial stages. (iii) The committee believes that the work of organizing teaching ought to demand whole-time attention, particularly in the early years of the school. (iv) Western Australia is faced with a number of special problems which can best be answered by the establishment of full-time heads of clinical departments. It strongly recommends the appointment of a professor of medicine with the assistance of a reader and a second assistant. Medicine, it is stated, is the parent discipline to surgery, pædiatrics and obstetrics; theoretical principles and practice are common to all. Medicine should be an all-embracing and integratory experience through which the student acquires a breadth of vision, and clarity and maturity of thought as well as factual information. It is thought that an active partnership should be formed between the department of medicine on the one hand and the State Departments of Health and Social Medicine and of Mental Health on the other, this partnership resulting in an integration in teaching between general principles and the actual practice of government departments in social and preventive medicine. In regard to surgery, it is stated that the task of organizing the teaching of the principles of surgery is perhaps less onerous than in medicine. The teaching could conceivably be done by one of Perth's senior consultant surgeons in a part-time capacity with the aid of a full-time first assistant or reader. A saving clause is added that if no one offers himself for appointment as head of the department of surgery, it will be necessary to appoint a full-time professor of surgery. The committee thinks that the desired teaching standards in child health can be attained only by the establishment of a chair in that subject. In making this recommendation, the committee is aware that the Board of Management of the Princess Margaret Hospital for Children wishes to see the establishment of a clinical research unit as part of the set-up. It is also aware that the trustees of the Queen Elizabeth II Coronation Gift Fund wish to spend money on increasing local knowledge of the care of mothers and babies. The professor of child health, it is stated, would be expected to organize teaching and to initiate investigational work, and also to act as a consultant to the Commissioner of Public Health. It is recommended that he should have a first assistant who would be a full-time hospital officer and whose salary was made up to the level of a senior lecturer by the university. The committee recommends the appointment of a professor of obstetrics, who, with his first assistant, would organize the teaching of obstetrics and gynæcology and would also advise the Public Health Department on the matters concerning maternal welfare in the State. In the matter of administration, it is thought that the aims of the school could best be served by the appointment of a part-time dean from the professorial board for a prescribed period. "In a new school it is better that decisions of policy should be solved by discussion in committee, rather than by edict of a full-time dean." A registrar or secretary should be responsible for the non-technical aspects of administration. After discussions between the committee and the various hospital boards, agreement was reached that teaching hospitals should have university representation on their boards of management and appointments committees. On the other hand, representatives of the honorary staffs of various hospitals would serve on senate appointment committees created to select clinical professors. The committee points out that in teaching hospitals a position on the honorary staff involves obligations towards students as well as towards "public" patients, a form of *noblesse oblige* dating from the origins of medical education itself. A portion of the formal teaching may be undertaken by members of the honorary staff "for which *pro rata* payment is conventional". The meeting ground between honorary staffs of hospitals and professorial departments is at the faculty, and to bind the team in unity the committee recommends the formation of curriculum committees of the faculty of medicine.

The parts of the report that have not been considered contain a wealth of detail which are interesting, but which are not really required in order that readers may gain a reasonable understanding of what is intended in Western Australia. The committee believes that the circumstances are very favourable to the establishment of this medical school. It points out that the numbers of students would not be excessive, that there is a wealth of clinical material, that individual tutorship would be possible, and that the school would begin with no preconceived ideas—it would be untrammelled by vested interests of long-established departments. The committee states that it would regard the school "beginning in temporary quarters, as a courageous experiment in medical education, in which unity of purpose, intelligent enthusiasm and far-sightedness, and contact with the practical medical problems facing Western Australia are factors contributing to good teaching which more than outweigh the absence of past tradition and of physical restrictions of old adapted buildings".

The most important point in this story is that the Government of Western Australia has accepted the report of the committee *in toto*. Some details, such as the fees to be charged, and so on, are still under discussion, but we may take it that a medical school is about to be established in Western Australia.

Current Comment.

THE PREERYTHROCYTIC STAGE OF MALARIA.

THE announcement by P. C. C. Garnham, R. S. Bray, W. Cooper, R. Lainson, F. I. Awad and J. Williamson[1,2] of their having demonstrated the preerythrocytic stage of *Plasmodium ovale* marks an occasion. In 1945, 1946 and 1947, Fairley, in the course of his investigations into the action

[1] *Brit. M. J.*, January 30, 1954.
[2] *Tr. Roy. Soc. Med. & Hyg.*, March, 1955.

of mepacrine and proguanil, provided evidence from which the existence of a preerythrocytic stage in human malaria could confidently be deduced. In January, 1948, Shortt and Garnham announced their findings of preerythrocytic forms of *P. cynomolgi* in the liver of *Macacus rhesus*; in March, 1948, they, together with Covell and Shute, reported having found the preerythrocytic stage of *P. vivax* in human liver. In 1949, Shortt, Fairley, Covell, Shute and Garnham reported the preerythrocytic stage of *P. falciparum* in human liver. In 1951, Garnham reported the preerythrocytic stage of *P. inui* in the liver of *Macaca mulatta*. And now the long task is almost completed—all that remains is to demonstrate the preerythrocytic stage of *P. malariæ* in human liver. Whether this can be achieved is doubtful, for *P. malariæ* presents far greater difficulties than any other species in the series, and the securing of a sufficient number of highly efficient mosquito vectors superinfected with a pure strain of this parasite might easily prove impossible. It was the brilliant conception of inducing colossal superinfection that made this work possible—in a natural infection the relatively few sporozoites which reach the liver give rise to such scattered preerythrocytic schizonts that the chance of finding one would be negligible even if there were any way of timing the search for one, and even if it could then be identified conclusively. It is only by infecting the subject with hundreds of thousands of sporozoites, so that the whole liver becomes so riddled with schizonts that a very small piece must inevitably contain several, that results can be obtained. But everything about *P. malariæ* is unfavourable to achieving the essential degree of superinfection.

Of course, it can be said with truth that the demonstration of the preerythrocytic stage of *P. malariæ* is now only of academic interest. In *P. cynomolgi* in the monkey we have the complete analogue of *P. vivax* in man; the pilot work on *P. cynomolgi* paved the way for the successful demonstration of *P. vivax*. There are no simian counterparts of *P. falciparum* or *P. ovale*, but the techniques which have been developed worked with perfect precision in demonstrating these species. *P. inui* in the monkey corresponds in every particular with *P. malariæ*, and has been fully demonstrated, so that parallel assumptions regarding *P. malariæ* are fully justifiable. Nevertheless, actual demonstration is highly desirable, and it is to be hoped that Dr. P. C. C. Garnham, who has been in the thick of this work from the start, may have the good fortune to round it off.

This work has contributed important facts of fundamental value to our knowledge of malaria. It has been achieved by original thinking, meticulous planning, and years of tedious work, heartened by generous cooperation and assistance of wide and international scope, and made possible by the selfless services of the human volunteers involved. Thus, in addition to the assistance rendered by schools of tropical medicine, large and busy hospitals, many laboratories, and departments of this and that, we read of a strain of *P. falciparum* from Professor Ciuca, of Bucharest, *A. quadrimaculatus* imported from the United States of America, a Malayan strain of *P. inui* obtained from the Malaria Institute of India, and many similar details. The strain of *P. ovale* which was used in the latest investigation was obtained in Liverpool, England, from a patient who had just returned from Liberia; it was first passaged, for therapeutic purposes, to a patient with Reiter's syndrome, and then to a patient with nephrosis. Thence it was inoculated into Garnham; seventeen days later, when he had developed a sufficiently high degree of parasitæmia, Lainson was sub-inoculated with his blood; Bray was sub-inoculated and used as a control; when Lainson developed gametocytæmia, 500 mosquitoes were fed from him, and when they became infectious they were allowed to bite Awad; finally, the strain was transferred to Williamson by mosquito bites, and he developed a sufficiently high density of gametocytes to superinfect 900 mosquitoes. Seven hundred and fifty of these were fed on Cooper; nine days later a liver biopsy was performed on him, and the preerythrocytic schizonts were demonstrated. These people, all volunteers, are members of the staff of the London School of Hygiene and Tropical Medicine—Cooper is the chief technician. In the vivax demonstration the subject was a patient in need of malaria therapy, who promptly agreed to having a liver biopsy done when the situation was explained to him. In the falciparum demonstration, the biopsy was done on a Mr. C. H. Howard, who had on his own initiative, out of his interest in malaria and his desire to benefit others, offered himself as a subject for experimentation; Mr. R. J. Bromfield, the subject of the secondary sub-inoculation experiments, volunteered for similar reasons. This sort of thing, of course, is continually going on among men of good will all over the world—we mention these particular names merely because they are relevant to the matter under discussion. Apart from its great scientific interest, the story of this work reminds us that materialism and selfishness have not become universal traits, as the Jeremiahs would have us believe.

X-RAY MACHINES FOR REMOTE PLACES.

A SURVEY made during the last few years revealed that throughout the South-West Pacific Area there were X-ray machines at most of the main centres, but that the radiographic facilities in general were not nearly adequate, and that the cost of installing enough extra machines to serve the area properly would be enormous and prohibitive without outside aid in most places. Recent developments, however, offer promise of simpler, smaller and cheaper machines. "Portable Isotopic X-ray Machine"[1] describes a unit powered by radioactive thulium which has been invented by Captain J. B. Storer and Corporal E. W. Coleman, of the United States Army. The complete unit, together with a special film folder, weighs only 48 pounds. A tiny piece of radioactive thulium is encased in a two-inch lead capsule with a shutter; the active life of the radioactivity of the thulium is about one year, after which it can be rejuvenated in an atomic pile for another year's service. The self-contained cassette holds pads soaked with developer and fixer, separated from a sheet of radiation-sensitive paper by slides which can be withdrawn after the paper has been exposed. The unit can be carried in a pack; the time for setting it up in the field and producing a completed picture is ten minutes; its cost is estimated at $200. The present model does not reproduce fine detail, but would apparently satisfy all field and emergency requirements.

Concurrently, J. F. Roach and H. E. Hilleboe[2] describe "Xeroradiography"; as a means of overcoming the difficulties of storing and processing X-ray film for emergency civil defence (considering among other things the effect atomic radiation would have on stored film), the authors have investigated and developed a photoelectric screen on which X-ray images can be projected. A metal plate has a thin sheet of the semiconductor selenium fused to one surface; it is then enclosed in a frame with a metallic cover slide. To prepare the plate for exposure, it is passed across a charging apparatus which carries a potential of 6000 volts and charges the selenium with positive ions. This static charge will endure for several hours; when the selenium is irradiated, those particles that are struck by the radiation become conductive, and pass their static charges through to the metal backing, which dissipates them homogeneously throughout its area. Within limits, at any point the proportion of the original charge that is dissipated into the backing plate is a direct measure of the quantity of radiation that strikes that point. The selenium is then sprayed with negatively charged powder, whose particles are attracted to those positive charges remaining on the selenium, a picture thereby being produced with a finely etched appearance, at least as fine in detail as a conventional X-ray film. The powder, in its pattern, can be transferred to paper by either an adhesive or an electrostatic technique for making a permanent

[1] *Med. Technicians Bull.* (*U.S.A.F. Med. J.*, supplement), March-April, 1955.

[2] *J.A.M.A.*, March 12, 1955.

record, or it can be brushed off and the plate can be recharged ready for re-use. The charging apparatus operates on 115 volts 60 cycles.

It is not impossible that when these two inventions have been developed commercially, they may between them offer to remote places all the advantages of radiography.

NEW ANTITUBERCULOSIS AGENTS.

ABOUT four years ago iso-nicotinic hydrazide or isoniazid was introduced for clinical trial in the treatment of tuberculosis. Other related compounds such as the 2-isopropyl derivative of isoniazid or iproniazid and derivatives of thiosemicarbazone have been introduced. Some very favourable results have been obtained with all these drugs, but severe toxic symptoms and a few deaths have followed their use. There is experimental evidence that these substances can replace nicotinamide in diphosphopyridine nucleotide (D.P.N.) which is essential for tissue oxidation. The substituted D.P.N. does not function in the cells as the parent substance. With accumulation of the substituted compounds symptoms of nicotinamide deficiency will occur.

V. C. Barry *et alii* in 1953 prepared oxidized polysaccharides such as starch, inulin and alginic acid and condensed them with isoniazid and *p*-aminobenzaldehyde thiosemicarbazone. The starch polymer with isoniazid was called hinstarch and that with the thiosemicarbazone was called constarch. Hinconstarch is a polymer of oxidized starch with isoniazid and the thiosemicarbazone condensed on alternate glucose residues.

V. C. Barry, M. L. Conalty and E. E. Gaffney[1] have investigated the activity of these substances in experimental tuberculosis. Some strains of *Mycobacterium tuberculosis* are resistant to isoniazid; both the resistant and the sensitive strains have been used in these experiments. The drugs were introduced in the food. Allowing for the weight of the sugar residues in these polymers, the activity was similar to, or in some cases higher than, the parent compounds in mice tuberculosis.

The constarch has considerable activity against the isoniazid-resistant strains of tubercle bacilli. Hinconstarch was remarkably effective in dealing with an infection due to isoniazid-sensitive strains and had considerable activity against the isoniazid-resistant strains. Hinconstarch was very active against established tuberculosis in guinea-pigs due to mixed strains. The toxicity of the polymers for mice was very low, much less than the equivalent of the parent substances. While these polymers have not been tried with human tuberculosis, there is evidence that they should prove a valuable addition to the antituberculosis drugs in current clinical use.

LATE CLINICAL CHANGES DUE TO RADIOACTIVE MATERIALS.

WITH the increasing use of radioactive materials and the deliberate or accidental introduction of these materials into the human body many questions are posed for which at present we have no satisfactory answers. One of much importance is concerned with the possible late effects of internally deposited radio-elements. W. B. Looney[2] has given a partial answer by studying individuals who, some considerable time ago, received radium medicinally or were luminous dial workers or who had received "Thorotrast" in diagnostic radiology ten to forty years previously. Radium was given intravenously or by mouth between the years 1915 to 1939 for the treatment of a variety of diseases. Fifty patients who had received radium during this period and 28 luminous dial workers who had been contaminated about 25 years before were examined. Radium storage in the body is closely analogous to the storage of lead in distribution and relation to calcium metabolism. We might then expect to find changes in the bones, and small areas of high focal concentration of radium were found irregularly distributed in the skeleton. These areas were usually about 5 to 15 microns in the greatest dimension. Atypical osseous tissue was found in the bone adjacent to these areas. Similar areas were found by X-ray examination—sometimes areas of increased density, giving a mottled appearance to the bone, sometimes areas of decreased density. Increased fragility of the bones also occurs, and skeletal malignant changes may develop 10 to 30 years after radium deposition. Fortunately the greater part of the radium introduced into the body is eliminated. Thorium dioxide ("Thorotrast") behaves quite differently. Almost all the administered "Thorotrast" is retained indefinitely. It is not much used now because of the formation of dense fibrotic reactions around sites of injection and the fear of carcinogenic effects from its radioactivity. "Thorotrast" is taken up by cells of the reticuloendothelial system; these form aggregates which become larger with increasing time following administration, but small amounts of thorium are found throughout the body. The only organ which may be much affected by the thorium accumulations is the spleen, the major part of the structure of which may be replaced by fibrous tissue. Changes have also been found in the liver, lymph nodes, adrenals, bone marrow and skeleton. Slight changes have been found on X-ray examinations of bone. Primary malignant disease of the liver was found in five patients and three cases of leuchæmia following the use of "Thorotrast", but no conclusions can be drawn from these as to the part played by the thorium. Nothing is known of the late effects of the several other radioactive elements which are now being used as diagnostic aids and in treatment, or which may enter the body accidentally. A careful watch should be kept for clinical findings which may be due to radioactivity in small doses over long periods. Very little is known of the length of time for which the newer radioactive elements remain in the body.

[1] *Brit. J. Urology*, March, 1955.
[2] *Ann. Int. Med.*, February, 1955.

A NEW ANTIBIOTIC FOR TYPHOID FEVER.

SOME typhoid fever patients, treated with chloramphenicol or tetracycline, and appearing to be promptly and completely cured, still suffer intestinal hæmorrhages or perforation, or, very rarely, necrotic parotitis, some twelve to twenty days after the onset of their illness. A reasonable explanation appears to be that the initial hyperæmia and hyperplasia in the Peyer's patches (or the parotid gland) was so severe and developed so rapidly before the diagnosis could be made and treatment started, that the mechanical basis for later necrosis was firmly established, so that no treatment could alter the subsequent progress of this process. Such complications are not so common, however, that a result of "no intestinal hæmorrhages, perforations, or deaths" in a series of only 15 cases is to be regarded as significant. On other counts, however, synnematin B has shown very promising results. L. Benavides V., B. H. Olson, G. Varela and S. H. Holt[1] have reported on the treatment of typhoid with synnematin B. Synnematin was found by Gottshall and co-workers in 1951, and separated into the A and B forms by Olson and his co-workers in 1953. The paper by Benavides and his colleagues reports the first clinical trial of synnematin B in human beings. Fifteen children suffering from typhoid fever and one with paratyphoid A were treated successfully, though three relapsed and in one the infection persisted for a long time. In all, the blood and fæces were finally cleared completely of *Salmonella typhi*, and none appeared to be carrying the infection when a survey was made three months later. It is to be hoped that the further trials which these workers intend to make will bear out the promise of this very good beginning.

[1] *J.A.M.A.*, March 19, 1955.

Abstracts from Medical Literature.

PÆDIATRICS.

Prognosis in Idiopathic Thrombocytopenic Purpura.

G. M. KOMROWER AND C. H. WATSON (*Arch. Dis. Childhood*, December, 1954) emphasize that there is a better prognosis for idiopathic thrombocytopenic purpura in childhood. Their own series consisted of 43 patients under the age of fifteen years. The condition of 24 was classed as "acute", that of seven as "indeterminate" (splenectomy was performed within four months of the onset) and that of the remainder as "chronic" (symptoms persisted for over six months). Six died, all within three weeks of onset of the condition; the remaining 18 patients in the acute group recovered within six months. Of the 12 patients in the chronic group none died. A history of a well-defined onset was usual in the acute, but not in the other groups. Spontaneous bleeding from more than one site and extensive ecchymoses occurred before the final hæmorrhage in the fatal cases. The presence of splenomegaly, urticaria, bone marrow eosinophilia exceeding 5% or very low platelet levels was without prognostic significance. A history of antecedent acute infection was obtained in 12 of 22 acute cases, and in four of the seven fatal cases, but in none of the chronic cases. In a review of 278 cases taken from the literature the authors found that 19 patients died, 17 within one month of onset of the condition. They suggest that those patients seen in the first month of illness, when the risks of splenectomy are great, should be treated with cortisone or corticotrophin, and that an expectant policy should be followed between the first and sixth months of the illness, splenectomy being reserved for those whose symptoms are increasing. After the first six months the decision to perform splenectomy should be based on the severity of the disability caused.

Radioiodine in Juvenile Myxœdema Due to Ectopic Thyroid Tissue.

E. M. MCGIRR AND J. H. HUTCHINSON (*Arch. Dis. Childhood*, December, 1954) used radioiodine in the investigation of two children with myxœdema. In one patient a mid-line swelling under the chin was excised when she was eleven years old in the belief that it was a thyroglossal cyst. Instead it was found to be thyroid tissue. After operation the child became very myxœdematous. After a dose of radioiodine minimal amounts of thyroid tissue were found by scanning with a Geiger-Müller counter in the region of the operative scar but nowhere else. The second patient, a dwarfed girl, seven years of age, had no palpable thyroid tissue, and the tongue looked normal. After radioiodine was given scanning of the neck with a Geiger-Müller counter showed that there was no thyroid tissue in the usual site, but that some was present at the base of the tongue just above the hyoid bone. In both children a surprising finding was that measurable amounts of radioiodine were present in the plasma, apparently as thyroxine, forty-eight hours after the ingestion of I^{131}. In myxœdema this is usually not the case, and it is suggested that a small amount of very active thyroid tissue may be responsible by causing a high turnover of available iodine. It is stated that the cases lend support to the opinion that hypothyroidism may result from a relative and progressive deficiency of thyroid hormone. The value is apparent of scanning the neck for I^{131} accumulations in unexplained juvenile myxœdema, and in patients with mid-line neck swellings.

A Fat Absorption Test with Iodized Oil.

F. N. SILVERMAN AND H. C. SHIRKEY (*Pediatrics*, February, 1955) have endeavoured to standardize a test for fat absorption depending on the liberation of iodine from lipiodol after absorption from the gut and the excretion of the iodine in the urine. Lipiodol in a dosage of not less than five millilitres, and of 0·5 millilitre per kilogram in children weighing between 10 and 20 kilograms, is given by mouth or stomach tube. Urine is tested for free iodine prior to giving lipiodol and between twelve and eighteen hours after giving it. After acidification with 8N nitric acid serial dilutions of urine are tested for the presence of free iodine by the addition of a freshly prepared 1% starch solution. Of 13 children with fibrocystic disease of the pancreas so tested, none showed a positive reaction for iodine in the urine in a dilution higher than 1 : 2, and in this dilution the reaction was positive in only two. Similarly deficient absorption of lipiodol was found in some of the 49 control children who were debilitated, a number because of diarrhœa. The authors consider that a positive result from the test for iodine after the ingestion of lipiodol in a dilution of urine of 1 : 4 or greater probably excludes fibrocystic disease of the pancreas as a diagnosis. A reaction consistent with the presence of fibrocystic disease of the pancreas warrants careful evaluation to determine its significance.

Secretory Otitis Media in Children.

S. S. SAMUELS (*Pediatrics*, March, 1955) states that the diagnosis of non-suppurative secretory *otitis media* has been made much more frequently in recent years. Usually the onset is acute, *otitis media* occurring during an upper respiratory tract infection. The usual progress of the *otitis media* may be halted by antibiotic treatment. Pain in the ear, a full sensation, deafness and the sound of bubbles in the ear are presenting symptoms. Commonly the syndrome is met with in children in whom adenoids or allergy are producing nasopharyngeal obstruction. Pain usually subsides as the infectious stage of the disease is brought under control by antibiotic therapy. Deafness of middle ear type persists, with the presence of a drum which is dull and opaque or generally red with absence of landmarks or which shows a fluid level. Treatment consists of relieving the nasopharyngeal obstruction by adenoidectomy or antiallergic measures and of removal of the fluid from the middle ear by paracentesis, with suction and tubal inflation if necessary. Recognition of the condition is important, so that effective treatment may be instituted and the process reversed before irreparable changes occur in the conducting mechanism.

Threadworms.

V. M. HOWIE (*Am. J. Dis. Child.*, February, 1955) treated 58 patients infested with *Enterobius vermicularis*. He administered piperazine hexahydrate in doses of 56 to 133 milligrammes per kilogram of body weight daily for ten consecutive days. Two weeks later seven consecutive daily perianal "Cellophane"-tape swabbings were examined; a cure was recorded if all seven showed negative results. By this criterion, 84% of the patients were cured of their infestation. Five patients showed symptoms of vertigo, which disappeared when the administration of the drug was discontinued.

Meconium Ileus.

C. B. OLIM AND A. CIUTI (*Ann. Surg.*, November, 1954) state that meconium ileus produces intestinal obstruction in the early newborn period. Very thick, tenacious meconium collects in the lower part of the ileum, where it adheres to the walls of the bowel, and to the surgeon's gloves and instruments when attempts are made to remove it. The obstruction produced is entirely mechanical in nature, owing to the gummy material present in the intestinal lumen. Only a short segment of ileum may be blocked by inspissated meconium, but more often the terminal 15 to 30 centimetres of ileum are obstructed. There are dilatation and distension of the obstructed segment of the ileum, which by its weight may undergo torsion and produce gangrene of the involved bowel. Gangrene and perforation may occur from pressure alone without torsion. Prior to 1948, the disease was uniformly fatal. Hiatt, in 1948, reported eight cases in which he had used saline instilled through an ileostomy wound, with a successful outcome in five cases. Gross had had no success with this method of removing the meconium and had with success resorted to a Mikulicz resection of the ileum containing the inspissated meconium, producing a double ileostomy; the ileostomies were closed in two to three weeks. The authors report two cases. In the first, when the patient was thirty-six hours old, laparotomy was performed, obstruction due to meconium ileus found, and the ileum opened. Saline was introduced through this ileostomy opening and an attempt made to express the meconium manually. The hopelessness of the situation became evident, and a solution of hydrogen peroxide (one part of 3% peroxide solution to three parts of water) was made. Ten millilitres of this were instilled into the ileum. The result was most spectacular; the meconium passed from the ileum as a large cast, apparently having been loosened from its contact with the mucosa of the ileum. This manœuvre was repeated several times, all meconium

cleared, and the ileostomy closed. The post-operative course was relatively smooth. The second infant was diagnosed as having a partial obstruction due to inspissated meconium in the colon. This was confirmed by retrograde lipiodol studies, and several enemata of similar peroxide of hydrogen solution were used to clear out the meconium plugs. Later stool tests confirmed the diagnosis of pancreatic cystic fibrosis.

Genetics of Gargoylism.

ROBERT C. CUNNINGHAM (*J. Neurol., Neurosurg. & Psychiat.*, August, 1954) reports 12 cases of gargoylism from the pedigree of a British family. All the subjects exhibited clear corneæ, low-grade defectiveness and normal skin. The pedigree demonstrates the presence of a sex-linked, recessive gene—males are exclusively affected. The average age at death was 8·7 years.

ORTHOPÆDIC SURGERY.

Advantages of the Knee Disarticulation over Amputations Through the Thigh.

J. W. BATCH, A. W. SPITTLER AND J. G. MCFADDIN (*J. Bone & Joint Surg.*, October, 1954) state that whenever an adequate below-the-knee stump cannot be obtained, a knee disarticulation is the next procedure of choice. The operative procedure is quick and safe and causes less shock than amputations through the thigh. The circulation in the thigh is preserved to supply skin flaps which are accustomed to pressure. Because muscle and bone are not transected, the spread of infection is minimized and the stump heals rapidly. When the patellar tendon has been fixed distally, patellar pain and swelling have not been significant problems. The largest surface available in the lower extremity is provided for weight-bearing. The stump is firm and insensitive. There is less atrophy of the muscles in the stump than after amputations at a higher level, and, because of this, earlier fitting of a prosthesis is possible. The shape of the stump provides greater balance and stability without rotation than that of stumps in higher amputations. The patient can walk with an excellent gait almost immediately. The prosthesis for such stumps is easy to construct and to fit, requires fewer adjustments and is superior to a prosthesis for higher levels of amputation through the thigh. Without a prosthesis the patient can kneel in work or play, bearing weight on the end of the stump in much the same way as the Symes amputee can on his longer stump. The authors conclude that knee disarticulation as a definitive procedure deserves the consideration of all orthopædic surgeons.

Digital Arthroplasty of the Proximal Interphalangeal Joint.

R. E. CARROLL AND T. H. TABER (*J. Bone & Joint Surg.*, October, 1954) state that there is a definite value in a surgical arthroplasty for the ankylosed proximal interphalangeal joint. They have operated upon 30 patients; in 16 cases the results were classed as good and in nine as fair; there were five failures. The longest period of follow-up has been seven years. The authors state that although it is generally believed that operation on the proximal interphalangeal joint produces an instable digit, this has not been their experience. They have found that arthroplasty is a valuable method of reconstruction for deformities of the proximal interphalangeal joint in selected cases. They did not attempt to replace the use and technique of joint arthrodesis in the flexed position of function. They state that criteria in the selection of cases must include ankylosis in a position of great deformity, no damage to the tendons which produce motion at the middle joint, and a high degree of motivation in the patient to regain mobility. The most simple technique, consisting in resection of the distal portion of the proximal phalanx, has been used. It is not necessary to use interposed tissue, metals or plastic material for the formation of the new joint. Skeletal traction has been maintained for six weeks. An active, closely supervised programme of rehabilitation has been found necessary. Of the first 30 patients there has been improvement in 83%. The authors hope to report better results in the future.

Cancellous Bone Grafts for Subacute and Chronic Osteomyelitis.

J. W. HAZLETT (*J. Bone & Joint Surg.*, November, 1954) has reviewed 101 cases of cancellous chip-bone grafting operations for filling of infected bone defects. Short-term follow-up showed primary or delayed primary healing in 87% of cases. Observation after five years revealed a recurrence rate of 20%. The recurrences were successfully overcome by minor procedures except in five patients, who suffer from repeated flare-ups of infection. At the present time, 91% of the lesions are satisfactorily healed with a partial or complete bone graft intact. There have been ten failures. The author states that statistical analysis has shown that *Proteus vulgaris* and *Bacillus pyocyaneus* are important causes of failure of the surgical procedure. These bacteria are not controlled by penicillin and sulphathiazole, which were the only two drugs used extensively in the cases of this series. It appears essential that the bacterial flora of an osteomyelitic lesion be controlled by antibiotics before a cancellous bone graft can be used with the assurance of a satisfactory result. The indications for a cancellous chip bone graft include osteomyelitic lesions that have caused a deep or large bone defect in an area of the body where sacrifice of considerable bone would be necessary to allow soft tissue closure. The criteria to be fulfilled for a successful cancellous chip bone graft in osteomyelitis are as follows: control of the infecting bacteria by antibiotics applied systemically or locally; full thickness skin coverage of the wound; complete removal of all infected bone and soft tissue; sufficient saucerization of bone and excision of soft tissue scar to expose a vascular bed for the bone grafts; decortication of the chip grafts; obliteration of all dead space by the loose packing of sufficient small bone chips; immobilization of the affected area to allow soft tissue healing or bony union of an associated fracture. When these criteria are satisfied, cancellous chip bone grafting for subacute or chronic osteomyelitis is a sound procedure, with a definite place in treatment.

Spondylolisthesis.

E. W. O. ADKINS (*J. Bone & Joint Surg.*, February, 1955) has operated on 46 patients with spondylolisthesis during the last five years. In all cases a thorough exploration was carried out in order to obtain a detailed picture of the anatomy of the lesion and in particular of the relations of the nerve roots. The author considers that backache is due to the instability of the affected segment, which increases the strains on the intervertebral ligaments and joints and ultimately causes severe localized osteoarthritis. The pains which radiate to legs are due to mechanical interference with the nerve root and cause the root compression syndrome or root irritation syndrome. In the irritation type the distribution of pain is exactly the same as in the compression syndrome, but physical signs are absent or slight. The author believes that the commonest cause of compression or irritation is a prolapsed or scarred disk. In cases of root irritation it was possible to show that interference with the nerve root occurred as it passed through the spinal canal and out of the intervertebral foramen. Of the 46 patients 38 had laminal defects. Of the 38 with defects 33 had definite slipping, and the remaining five had typical defects of the *pars articularis* of the lamina but no slip. The author was unable to throw much light on the origin of the defects within the isthmus. He believes that at least in several cases both the defects and the slipping must have been present at a very early stage of skeletal development, because laminal defect was much narrower than the step between the vertebral bodies, and this was brought about by elongation of the posterior part of the isthmus. He advocates operation to explore the defect, decompress the nerve roots and arthrodese the affected area. The loose lamina is completely removed, together with the attached inferior facets and with *ligamentum flavum* above and below. The author advocates preliminary spinal anæsthesia to diminish the bleeding without which really adequate exploration is impossible. When the lamina has been removed, the pseudarthrosis itself is dealt with after any adhesions between it and the nerve root have been separated. The author points out that all the tissue filling in the defect must be nibbled away. The anterior part of the isthmus must then be removed until the root is seen to be lying quite freely as it curves round the antero-medial border of the pedicle. Because leg pain has recurred in about one-fifth of the patients, the author now believes that whenever possible the sensory nerve root should be divided. It is pointed out that the usual methods of bone graft in the lumbo-sacral region, especially after laminectomy, result in many failures to obtain bony fusion. The author advocates intertransverse or alatransverse grafts rather than posterior or intercorporal grafts.

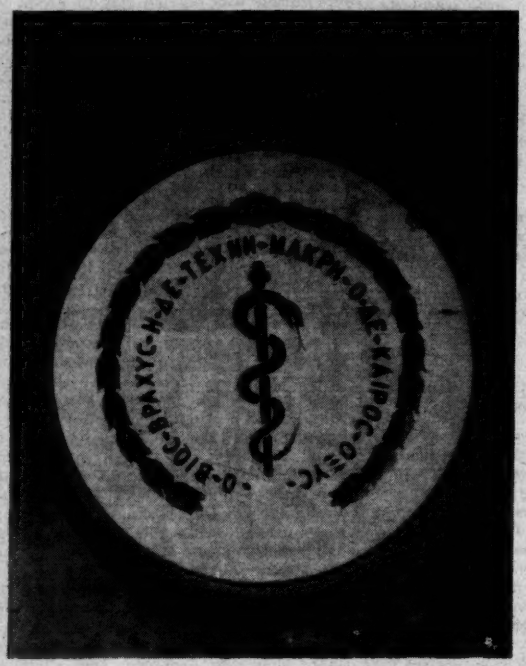
British Medical Association News.

ANNUAL MEETING.

THE annual meeting of the New South Wales Branch of the British Medical Association was held at the Robert H. Todd Assembly Hall, British Medical Association House, 135 Macquarie Street, Sydney, on March 31, 1955, DR. T. Y. NELSON, the President, in the chair.

PRESENTATION OF PRESIDENT'S BADGE.

Dr. Angus Murray announced that for some time certain members of the Branch had wished to see the President of the Branch wear a presidential badge when he presided at



Branch functions. He explained that a badge had been prepared and he asked the President to accept it on behalf of the donors. The donors were Dr. Edgar Thomson, Dr. W. F. Simmons, Dr. T. Y. Nelson, Dr. Mervyn Archdall and himself. Dr. Murray then invested the President with the badge. The President accepted the badge on behalf of the Council and members and thanked the donors for their gift. The badge had been cast in gilded metal and was decorated with coloured enamel. A picture of the obverse and the reverse of the badge is published herewith.

ANNUAL REPORT OF COUNCIL.

The annual report of the Council was received on the motion of Dr. H. R. R. Grieve, seconded by Dr. Edgar F. Thomson. After the report had been shortly commented on by the President, it was adopted on the motion of Dr. H. R. R. Grieve, seconded by Dr. Edgar Thomson. The report is as follows.

The Council presents the following report on the work of the Branch for the year ended March 31, 1955.

Membership.

The membership of the Branch is now 3804, as against 3695 at the date of the last report. The additions have included 228 elections, re-elections and resumptions, and 89 removals into the area of the Branch; while the losses have included 24 by resignation, 124 removals out of the area of the Branch, 23 by default in payment of subscription, and 37 by death. The losses by death were as follows: Dr. J. C. Binns, Dr. G. H. Walton Smith, Dr. Addie Walker, Dr. C. P. Ley, Sir Robert Wade, K.B., Dr. J. McD. Mack, Dr. A. E. Harker, Dr. R. G. V. Shaw, Dr. J. A. Kennedy, Dr. P. A. Sheehan, Dr. Del Potter, Dr. A. W. J. Stocks, Dr. Mary H. K. Wallace, Dr. C. G. Roberts, Dr. J. M. Skype, Dr. R. J. B. McEwen, Dr. R. M. Glasson, Dr. W. E. Giblin, M.C., Dr. W. T. Nelson, Dr. E. A. Brearley, Dr. E. A. Seagar, Dr. W. M. A. Fletcher, Dr. P. J. Stormon, Dr. H. F. Alsop, Dr. M. K. Stevenson, Dr. H. St. J. Saunders, Dr. R. P. Lockley, Dr. Katie Ardill-Brice, O.B.E., Dame of St. John, Dr. C. A. F. Clark, Dr. A. M. Davidson, O.B.E., Dr. H. Pearlman, Dr. J. J. Hollywood, Dr. A. H. Hart, Dr. G. P. Arnold, Dr. E. A. R. Bligh, Dr. H. G. McQuiggin, Dr. E. Huth.

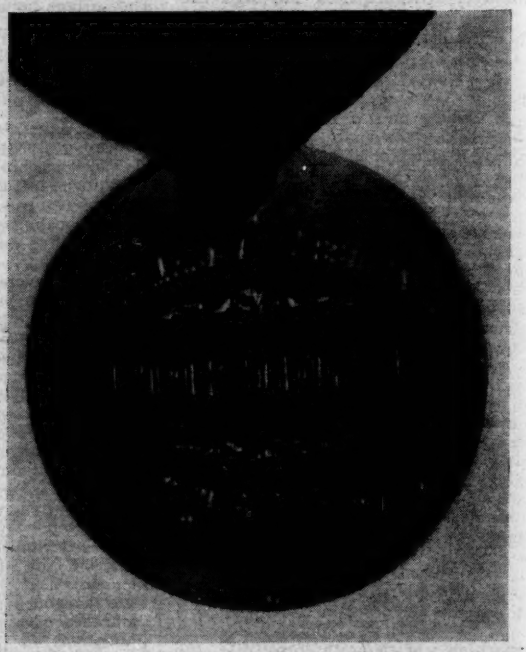
Obituary: Arthur Madgwick Davidson.

The Branch has suffered by the death on January 20, 1955, of Dr. Arthur Madgwick Davidson, O.B.E. A member of the Council from 1930 to 1946, he was President in 1935, and in the same year represented the Branch at a meeting of the Federal Council. He was also a director of the Australasian Medical Publishing Company, Limited, for eleven years. The deep sympathy of the Branch is extended to his family.

War Memorial, World War, 1939-1945: Roll of Honour.

A roll of honour, erected on the first floor of British Medical Association House, to commemorate the names of those members of the medical porfession in New South Wales who gave their lives in World War II, 1939-1945, was unveiled by His Excellency the Governor of New South Wales, Lieutenant-General Sir John Northcott, K.C.M.G., K.C.V.O., C.B., on Sunday, June 27, 1954.

The roll of honour in the form of a tablet contains the names of thirty-nine members who gave their lives. It is a replica of the tablet erected in the old building in Elizabeth Street to commemorate the names of those who



gave their lives in the 1914-1918 war. This tablet was subsequently transferred to British Medical Association House following the completion of the building. The two tablets now face each other on the first floor landing.

The President, Dr. T. Y. Nelson, opened the meeting and called upon the Medical Secretary to read the list of the thirty-nine names inscribed on the tablet. An address was then given by His Excellency the Governor and this was followed by the unveiling. The ceremony concluded with the sounding of "The Last Post" and "Reveille".

Congratulations.

Congratulations were extended to Sir Archibald Collins, K.B., D.S.O., M.C., President of the Federal Council of the British Medical Association in Australia and Vice-President of the New South Wales Branch, and to Sir

Herbert Schlink, K.B., following the conferring upon each of them of a knighthood by Her Majesty the Queen. Congratulations were also extended to Dr. A. J. Metcalfe, C.B.E., Dr. Moya Blackall, M.B.E., Dr. C. J. M. Walters, C.B.E., and Dr. R. S. Steel, O.B.E., on the honours conferred on them by Her Majesty the Queen.

Meetings.

Ten ordinary general meetings of the Branch (including the annual general meeting), one extraordinary general meeting of the Branch, and nine clinical meetings were held; the average attendance was 70.

Six ordinary general meetings were held in conjunction with meetings of the special groups, namely; April 29, with the Section of Medicine and the Section of Obstetrics and Gynæcology; May 27, with the Section of Medicine and the Section of Neurology, Psychiatry and Neurosurgery; July 29, with the Section of Neurology, Psychiatry and Neurosurgery; August 26, with the Section of Pædiatrics and the Section of Obstetrics and Gynæcology; September 30, with the Section of Radiology and the Section of Obstetrics and Gynæcology; December 9, with the Section of Medicine and the Australian Association of Physical Medicine. Sixteen papers were presented at these meetings.

The clinical meetings were held at the Rachel Forster Hospital for Women and Children, Royal North Shore Hospital, Royal Prince Alfred Hospital, Royal Alexandra Hospital for Children, Saint Vincent's Hospital, Lewisham Hospital, Sydney Hospital, Royal Hospital for Women, and Saint George Hospital.

At the ordinary general meeting on June 24 a paper on "Changes in Infectivity of Infectious Diseases" was presented by Dr. H. McLorinan, Medical Superintendent, Fairfield Hospital, Melbourne, and at the ordinary general meeting on November 25 Dr. J. C. Fulton presented a paper on "Hospital Records".

By-law 4 (annual subscription) was redrafted at the extraordinary general meeting held on Decemer 9. The redrafted by-law did not alter the existing rates of subscription.

The third Branch meeting in a country town was held at Tamworth on Saturday and Sunday, October 30 and 31, two papers being read. In addition to a scientific programme, social functions and sporting events were arranged by the Northern District Medical Association. The Council extends its grateful thanks to the Northern District Medical Association for its assistance in the organization of the meeting.

An invitation was extended to members of the legal profession to be present at the ordinary general meeting held on July 29, when a paper was presented by Dr. J. A. H. McGeorge on "Medico-Legal Aspects of Psychiatry". An invitation was extended to the fifth and sixth year medical students of the University of Sydney to attend ordinary general meetings and to sixth year medical students to attend clinical meetings of the Branch.

Representatives.

The Branch was represented as follows:

1. Council of the British Medical Association (1955-1958): Dr. Isaac Jones.
2. Annual Representative Meeting, British Medical Association, Glasgow, July, 1954; Representatives, Dr. J. N. Chesterman, Dr. E. Murray-Will, Dr. C. W. S. Dun.
3. Federal Council of the British Medical Association in Australia: Sir Archibald Collins, K.B., D.S.O., M.C., Dr. A. J. Murray, O.B.E., Dr. W. F. Simmons, Dr. H. R. R. Grieve.
4. Australasian Medical Publishing Company, Limited: Dr. W. F. Simmons, Dr. W. L. Calov, Professor L. F. Dods, M.V.O.
5. New South Wales Post-Graduate Committee in Medicine: Dr. A. C. Thomas, Dr. E. F. Thomson, Dr. S. R. Dawes.
6. The Ophthalmic Association Limited: Dr. E. V. Waddy Pockley.
7. The Flying Doctor Service of Australia: Dr. George Bell, O.B.E.; Deputy Representative, Dr. J. G. Hunter.
8. Council of the Bush Nursing Association: Dr. T. Y. Nelson.
9. Hospitals Contribution Fund of New South Wales: Dr. Hugh Hunter.
10. St. John Ambulance Association: Dr. T. Y. Nelson.
11. Standards Association of Australia: (i) Institutional Supplies Committee, Dr. S. W. G. Ratcliff; (ii) Sectional Committee on Interior Illumination of Buildings, Dr. J. Davis; (iii) Committee on Standards of Laboratory Glassware and Volumetric Glassware, Dr. F. S. Hansman; (iv) New South Wales Committee on Protective Occupational Clothing, Dr. W. T. Nelson; (v) Paint and Varnish Subcommittee No. 8, Dr. W. T. Nelson; (vi) New South Wales Committee on Eye Protection, Dr. J. Davis; (vii) Sectional Committee on Measuring Cups and Spoons, Dr. W. W. Ingram; (viii) New South Wales Committee on Industrial Respiratory Protective Devices, Dr. W. E. George.
12. Medical Officers' Relief Fund (Federal): Local Committee of Management for New South Wales, Dr. A. M. McIntosh, Dr. A. J. Murray, O.B.E., Sir Archibald Collins, K.B., D.S.O., M.C.
13. Medical Appointments Advisory Committee (Hospitals Commission of New South Wales): Dr. B. T. Edye.
14. Special Departmental Committee for the Investigation of Maternal Deaths: Dr. E. A. Tivey; Alternate Representative, Dr. M. H. Eliot-Smith.
15. Recreation and Leadership Movement: Professor Harvey Sutton.
16. Council of the New South Wales Institute of Hospital Almoners: Dr. R. A. R. Green.
17. New South Wales Medical Board: Dr. J. R. Ryan.
18. New South Wales Examining Council for Medical Technology (Hospitals Commission of New South Wales): Dr. E. F. Thomson, Dr. F. S. Hansman.
19. Medical Finance Limited, Board of Directors: Dr. E. A. Tivey, Dr. A. C. Thomas, Dr. George Bell, O.B.E., Dr. G. C. Halliday.
20. Council of the New South Wales Institute of Dietitians: Dr. K. S. Harrison.
21. Coordinating Council of the Physically Handicapped: Dr. R. A. R. Green.
22. Road Safety Council of New South Wales: Dr. T. Y. Nelson.
23. Road Safety Council of New South Wales (i) Committee to examine and report on matters dealing with road accidents involving motor cycles: Dr. I. D. Miller.
24. Federal Medical War Relief Fund, Local Committee of Management: Sir Archibald Collins, K.B., D.S.O., M.C., Dr. A. C. Thomas, Dr. A. J. Murray, O.B.E.
25. Florence Nightingale Memorial Committee of Australia: Dr B. T. Edye.
26. National Association for the Prevention of Tuberculosis in Australia (New South Wales Division): Dr. W. Cotter B. Harvey.
27. Committee for Placement of Resident Medical Officers: Dr. A. M. McIntosh.
28. Australian Physiotherapy Association: Dr. B. G. Wade.
29. The Cavalcade of Nursing Committee: Dr. H. R. R. Grieve.
30. New South Wales State Cancer Committee and Cancer Advisory Committee: Dr. B. T. Edye.
31. Council of the Pædiatric Association, Limited: Dr. G. L. Howe.
32. Department of Motor Transport (Committee to consider the question of the adoption of chemical tests of body fluids to determine whether a driver is under the influence of alcohol): Dr. F. S. Hansman.
33. Chiropody Board of New South Wales: Dr. T. Y. Nelson, Dr. S. H. Scougall, Dr. R. F. A. Becke.
34. Medico-Pharmaceutical Liaison Committee: Dr. J. K. Maddox, Dr. G. L. Howe, Dr. W. F. Simmons, Dr. J. G. Hunter.
35. Department of Public Health, Poisons Advisory Committee: Dr. A. W. Morrow, D.S.O.
36. National Health Service, Pensioner Medical Service, Committee of Inquiry: Dr. M. S. Alexander, O.B.E., Dr. B. A. Cook, Dr. A. W. Morrow, D.S.O., Dr. A. C. Thomas.
37. State Medical Advisory Committee: Dr. E. F. Thomson; Alternate Representative, Dr. J. G. Hunter.
38. Fluoridation of Drinking Water, Department of Public Health Advisory Committee: Dr. D. G. Hamilton.

Council.

(a) The attendance of members of the Council and of the standing committees was as set out in the accompanying table.

(b) The representatives of the Local Associations of members appointed on the invitation of the Council to attend the regular quarterly meetings of the Council were as follows: Dr. L. Bamber (Blue Mountains), Dr. H. M. Webber (Border), Dr. Franziska Schlink (Broken Hill), Dr. J. Adrian Paul (Brisbane Water District), Dr. L. Abramovich (Canterbury-Bankstown), Dr. T. W. Edmeades (Central Northern), Dr. B. W. Monahan (Central Southern), Dr. K. S. M. Brown (Central Western), Dr. A. McNeil (Eastern District), Dr. J. R. Sands (Eastern Suburbs), Dr. E. C. Blomfield (Far South Coast and Tablelands), Dr. W. A. Conolly (Hunter Valley), Dr. G. W. Ashby (Illawarra Suburbs), Dr. T. M. Clouston (Kuring-gai District), Dr. J. R. Ryan (North Eastern), Dr. H. G. Royle (Northern District), Dr. John Maude (South Eastern), Dr. J. Oliver (Southern District), Dr. K. A. Barr (South Sydney), Dr. R. G. Bligh (Warringah District), Dr. G. B. Downes (Western), Dr. Warren Smith (Western Suburbs).

Library.

Dr. A. M. McIntosh was appointed to the position of Honorary Librarian.

Visitors to the Library	6639
Books lent to members	1187
Journals lent to members	4163
Books added to the Library	152
Journals added to the Library	9

A comparison with last year's figures will show a slight decrease in the number of visitors to the Library, but this has undoubtedly been brought about by the increase in the interlibrary loans (approximately 750 publications), as a result of which members can obtain their material through hospital libraries *et cetera*, where in most cases a messenger service is available.

The number of items borrowed from other libraries was approximately 75, and it is the desire of the Association to place on record its appreciation of the assistance rendered by those libraries who were contacted for the purpose of obtaining information and material not available in the Branch Library.

The use of the photocopying service is rapidly increasing and during the period under review 102 articles were photographed, representing a total of 764 prints.

A revised and enlarged catalogue of the Library's holdings since 1938 is being compiled, and lists of duplicate periodicals and books are being prepared for circulation to allied and scientific libraries.

The Association is pleased to record its grateful thanks for donations received from the following: the Editor, THE MEDICAL JOURNAL OF AUSTRALIA; American College of Surgeons; American Hospital Association; British Medical Agency; Dr. Grace J. Browne; Dr. G. S. Colvin; Commissioner of Public Health, Perth, Western Australia; Dr. V. M. Coppleson; Dr. H. J. Daly; Dr. H. C. Rutherford Darling; Dr. J. A. Flynn; Dr. J. Foley; Professor E. Ford; Dr. W. C Gibson (through Dr. Stephen Lynch); Dr. J. Heyman, Stockholm; Dr. E. M. Humphery; Library of the Faculty of Medicine, University of Western Ontario; Professor Ida Mann; Medical and Chirurgical Faculty of the State of Maryland Library; Dr. A. M. McIntosh; Nagoya City University Medical School; National Health and Medical Research Council; National Institutes of Health Library, Bethesda, Maryland; National Vitamin Foundation, New York; New England University Library; Postgraduate Committee in Medicine, University of Sydney; Dr. Ian Potts; Prince Henry Hospital; Public Health Department of New South Wales; Dr. A. E. Rowden-White; Royal Australasian College of Physicians; Saint Vincent's Hospital; Dr. R. J. Silverton; Southmead General Hospital, Bristol, England; Stanford University (Lane Medical Library), California; Dr. K. W. Starr; Dr. F. G. N. Stephens; Dr. E. F. Thomson; United States Armed Forces Library; United States Information Library; University of Texas Medical Branch Library; Vanderbilt University School of Medicine Library, Tennessee; the College of Radiologists (Australia and New Zealand); the Oto-Rhino-Laryngological Society of New South Wales (British Medical Association); the Section of Medicine, the Section of Obstetrics and Gynæcology, and the Dermatological Association of Australia (British Medical Association).

Details of the amount expended on the Library for the year ended December 31, 1954, are as follows:

Salaries	£1688	7	1
Subscriptions for journals	800	8	0
Books	459	4	7
Binding	453	19	3
Equipment	7	7	4
	£3409	6	3

This amount, £3409 6s. 3d., absorbed 14·7% of the net subscriptions received.

Affiliated Local Associations of Members.

Blue Mountains (affiliated 1944): *Chairman*, Dr. A. H. Macintosh; *Honorary Secretary*, Dr. N. Larkins. Membership 30. Four meetings were held.

ATTENDANCE AT COUNCIL AND STANDING COMMITTEE MEETINGS.

	Council.	Committees.				
		Executive and Finance.	Organization and Science.	Medical Politics.	Hospitals.	Ethics.
ALEXANDER, M. S.	10	—	—	11	—	—
BELL, GEORGE. Honorary Treasurer	10	12	5	8	2	3
BLACKBURN, SIR CHARLES	6	—	—	—	—	3
COLLINS, SIR ARCHIBALD. Vice-President	6	—	—	1	—	2
COOK, B. A.	7	—	—	—	3	—
DRAKIN, J. E. F.	10	—	—	11	5	—
EDYE, B. T.	10	—	—	—	—	3
GRIEVE, H. R. R. Honorary Secretary	10	11	3	7	1	2
HALLIDAY, G. C.	9	—	—	—	—	2
HOWE, G. L.	9	9	—	—	—	—
JOHNSON, A. S.*	4	5	4	—	—	—
JONES, K. S.	9	—	—	10	—	—
LITTLE, J. P.	4	—	—	8	—	—
MACDONALD, R. H.	8	—	—	—	—	3
MORROW, A. W.	6	—	2	—	2	—
MURRAY, A. J. Past President	9	12	—	—	—	—
NELSON, T. Y. President	10	12	7	11	5	3
RAWLE, K. C. T.	4	—	—	—	0	—
SIMMONS, W. F.	10	11	—	10	—	—
SOLLING, F. P. M.*	6	—	—	6	—	—
STUCKEY, R. S.	10	—	—	10	—	—
TAYLOR, HELEN M.	8	—	5	—	—	—
THOMSON, E. F.	9	9	6	—	—	—
TURNBULL, H. I.	8	—	—	—	3	—
WILLIS, H. H. President Elect	10	9	7	13	5	3
Meetings held	10	12	7	13	5	3

* Leave of absence from November, 1954, to January, 1955.

Border (affiliated 1908): *Chairman*, Dr. L. S. Woods; *Honorary Secretary*, Dr. H. M. Webber. Membership 18. Three meetings were held.

Brisbane Water District (affiliated 1948): *Chairman*, Dr. A. J. Harmey; *Honorary Secretary*, Dr. G. C. Duncan. Membership 18. Four meetings were held.

Broken Hill (affiliated 1942): *Honorary Secretary*, Dr. Franziska Schlink.

Canterbury-Bankstown (affiliated 1930): *Chairman*, Dr. K. Byrne; *Honorary Secretary*, Dr. F. Wishaw. Membership 71. Four meetings were held.

Central Northern (affiliated 1910): *Chairman*, Dr. L. N. Ferrari; *Honorary Secretary*, Dr. H. W. Rundle.

Central Southern (affiliated 1909): *Chairman*, Dr. E. B. Docker; *Honorary Secretary*, Dr. F. B. Uther. Membership 64. Four meetings were held.

Central Western (affiliated 1910): *Chairman*, Dr. A. R. Woolnough; *Honorary Secretary*, Dr. K. S. M. Brown. Membership 78. Four meetings were held.

Eastern District (affiliated 1913): *Chairman*, Dr. F. W. Baylon; *Honorary Secretary*, Dr. A. McNeil. Membership 41. Three meetings were held.

Eastern Suburbs (affiliated 1911): *Chairman*, Dr. W. T. Whitby; *Honorary Secretary*, Dr. J. G. Radford. Membership 147. Six meetings were held.

Far South Coast and Tablelands (affiliated 1935): *Chairman*, Dr. J. F. Ireland; *Honorary Secretary*, Dr. E. C. Blomfield. Membership 14. Three meetings were held.

Hunter Valley (affiliated 1947): *Chairman*, Dr. F. P. M. Solling; *Honorary Secretary*, Dr. D. W. Lawson. Membership 44. Seven meetings were held.

Illawarra Suburbs (affiliated 1913): *Chairman*, Dr. K. W. Alexander; *Honorary Secretary*, Dr. G. W. Ashby. Membership 121. Six meetings were held.

Kuring-gai District (affiliated 1929): *Chairman*, Dr. N. F. Babbage; *Honorary Secretary*, Dr. R. C. White. Membership 103. Four meetings were held.

Northern District (affiliated 1911): *Chairman*, Dr. J. L. Watt; *Honorary Secretary*, Dr. H. G. Royle. Membership 80. Three meetings were held.

North Eastern (affiliated 1913): *Chairman*, Dr. J. Gribben; *Honorary Secretary*, Dr. N. J. Rogers. Membership 65. Four meetings were held.

Southern District (affiliated 1909): *Chairman*, Dr. J. S. Storey; *Honorary Secretary*, Dr. J. L. Tunley. Membership 28. Two meetings were held.

South Eastern (affiliated 1941): *Chairman*, Dr. B. A. Cook; *Honorary Secretary*, Dr. N. J. Powrie. Membership 61. Nine meetings were held.

South Sydney (affiliated 1909): *Chairman*, Dr. T. K. Potts, junior; *Honororay Secretary*, Dr. K. A. Barr.

Warringah District (affiliated 1929): *Chairman*, Dr. E. S. Stuckey; *Honorary Secretary*, Dr. R. T. C. Hughes. Membership 164. Six meetings were held.

Western (affiliated 1908): *Chairman*, Dr. A. E. Lorger; *Honorary Secretary*, Dr. S. R. Dawes. Membership 104. Three meetings were held.

Western Suburbs (affiliated 1908): *Chairman*, Dr. D. B. Wightman; *Honorary Secretary*, Dr. Warren Smith. Membership 128. Six meetings were held.

Annual Meeting of Delegates.

The forty-first annual meeting of delegates of the affiliated local associations of members with the Council was held on Friday, October 1, 1954.

The delegates present at the meeting were as follows: Border, Dr. H. M. Webber; Broken Hill, Dr. W. B. Dorsch; Brisbane Water District, Dr. J. Adrian Paul; Canterbury-Bankstown, Dr. L. Abramovich; Central Northern, Dr. T. W. Edmeades; Central Southern, Dr. B. W. Monahan; Eastern District, Dr. A. McNeil; Eastern Suburbs, Dr. L. H. McMahon; Hunter Valley, Dr. L. O. Rutherford; Illawarra Suburbs, Dr. G. W. Ashby; Kuring-gai District, Dr. C. Warburton; North Eastern, Dr. J. L. Roberts; Northern District, Dr. R. J. Jackson; South Sydney, Dr. C. H. Jaede; Southern District, Dr. J. S. Storey; Warringah Distriet, Dr. R. G. Bligh; Western, Dr. G. B. Downes; Western Suburbs, Dr. Warren Smith.

Special Groups for the Study of Special Branches of Medical Knowledge.

Allergy (inaugurated 1947); *Chairman*, Dr. R. S. Steel; *Honorary Secretary*, Dr. Bernard Riley. Membership 12. Four meetings were held.

Anæsthesia (inaugurated 1934): *Chairman*, Dr. L. T. Shea; *Honorary Secretary*, Dr. R. B. Speirs. Membership 53. Five meetings were held.

Medicine (inaugurated 1924): *Chairman*, Dr. F. Hales Wilson; *Honorary Secretary*, Dr. J. Isbister. Membership 83. Seven meetings were held, three in conjunction with meetings of the Branch.

Neurology, Psychiatry and Neurosurgery (inaugurated 1924): *Chairman*, Dr. K. B. Noad; *Honorary Secretary*, Dr. J. L. Evans. Membership 99. Eleven meetings were held, two in conjunction with meetings of the Branch.

Obstetrics and Gynæcology (inaugurated 1925): *Chairman*, Dr. F. N. Chenhall; *Honorary Secretary*, Dr. F. A. Bellingham. Membership 107. Seven meetings were held, three in conjunction with meetings of the Branch.

Occupational Medicine (inaugurated 1952): *Chairman*, Dr. M. R. Finlayson; *Honorary Secretary*, Dr. G. C. Smith. Membership 28. Five meetings were held.

Orthopædic Group (British Medical Association) (inaugurated 1923): *Chairman*, Dr. W. Stening; *Honorary Secretary*, Dr. A. R. Rhydderch. Membership 29. Five meetings were held.

Oto-Rhino-Laryngological Society of New South Wales (inaugurated 1924): *Chairman*, Dr. L. S. Corner; *Honorary Secretary*, Dr. T. H. O'Donnell. Membership 36. Three meetings were held.

Pædiatrics (inaugurated 1924): *Chairman*, Professor Lorimer Dods; *Honorary Secretary*, Dr. S. E. J. Robertson. Membership 102. Six meetings were held, one in conjunction with a meeting of the Branch.

Pathology (inaugurated 1924): *Chairman*, Dr. J. M. Garvan; *Honorary Secretary*, Dr. J. L. Holme. Membership 93. Six meetings were held.

Radiology (inaugurated 1926): *Chairman*, Dr. D. G. Maitland; *Honorary Secretary*, Dr. E. W. Frecker. Membership 98. Six meetings were held, one in conjunction with a meeting of the Branch.

Surgery (inaugurated 1925): *Chairman*, Dr. V. M. Coppleson; *Honorary Secretary*, Dr. Alan Sharp. Membership 56. One meeting was held.

Urology (inaugurated 1940): *Chairman*, Dr. D. C. Trainor; *Honorary Secretary*, Dr. H. G. Cummine.

Australasian Medical Congress (British Medical Association), Ninth Session, Sydney, August 20-27, 1955.

The organization of the Australasian Medical Congress, which is the responsibility of the New South Wales Branch, is well on its way.

The tentative programme provides for the inaugural meeting to be held in the Sydney Town Hall on the evening of August 22, when the President's address will be given by Sir Archibald Collins.

The meeting will be opened by His Excellency the Governor-General of Australia, Field Marshal Sir William Slim, G.C.B., G.C.M.G., G.B.E., D.S.O., M.C.

The Henry Simpson Newland Oration will be delivered in the Great Hall of the University of Sydney on the evening of Thursday, August 25, by Dr. Louis H. Bauer, Secretary-General of the World Medical Association and a Past President of the American Medical Association. The main plenary session on "Cancer" will be held on the morning of Tuesday, August 23, and four other plenary sessions on "Control of Infectious Diseases", "Rehabilitation", "The Use and Abuse of Hormones in Medical Practice", and "Industrial and Occupational Hazards to Health" on the afternoon of the same day.

Combined meetings of sections will be held on Wednesday, August 24, and meetings of sections on Thursday, August 25, and Friday, August 26.

The congress dinner will be held on the evening of Wednesday, August 24, and the New South Wales Branch ball will be held on the evening of Friday, August 26.

In addition, many private parties will be provided by members and their wives, the arrangement of these being in the hands of the Ladies' Committee.

Federal Council of the British Medical Association in Australia.

The Federal Council of the British Medical Association in Australia met in Brisbane on August 30–September 1, 1954, in Canberra on October 28, 1954, and in Melbourne on February 14–16, 1955.

The Branch was represented at each meeting by Sir Archibald Collins, Dr. H. R. R. Grieve, Dr. A. J. Murray and Dr. W. F. Simmons.

British Medical Association Lectures.

Lectures were arranged as follows:

Eastern District Medical Association, Port Macquarie, May 16, 1954. Dr. D. M. Ross, "The Integration of Psychiatry with Internal Medicine".

Northern District Medical Association, Armidale, September 19, 1954. Dr. H. M. Rennie, "Minimal and Asymptomatic Pulmonary Tuberculosis Lesions".

Annual Branch Prize for an Essay on a Scientific Subject.

The subject chosen for the Annual Branch Prize for an essay on a scientific subject for the year 1955 is "Panhysterectomy—Its Effect on the Individual".

It is to be regretted that there were no entries for the year 1954, when the subject was "The Present-day Pattern of Infectious Diseases".

The prize is 100 guineas and a bronze medallion. The essay must not exceed 12,000 words.

National Health Act.

All sections of the *National Health Act* have been proclaimed and are now in operation. Medical benefits, pensioner medical benefits, hospital benefits and pharmaceutical benefits are available to the community.

Strong protests were made against the introduction of regulations governing the provision of pharmaceutical benefits without prior reference to the medical profession.

During the year discussions took place between the Federal Council and the Commonwealth Government in regard to the Pensioner Medical Service and the liberalization of the means test. In order that it would be in a position to advise the Federal Council of the views of the New South Wales Branch, the Council, at the end of September, 1954, submitted certain proposals of the Government and the Federal Council to local associations for their consideration.

Fees Payable to Legally Qualified Medical Practitioners for Services Rendered on Behalf of the Government.

As a result of representations made by the Council, amendments were made to the regulations governing the fees payable to legally qualified medical practitioners for services rendered on behalf of the Government on request. These amendments provide for increases in a number of the fees in the regulations.

Hospital Policy.

A great deal of consideration has been given by Council to the hospital policy of the Association during the year.

Representations have been made to the Minister for Health and the Hospitals Commission of New South Wales stressing the need for a more satisfactory classification of patients and an extension of the number of private and intermediate beds.

NEW SOUTH WALES BRANCH OF THE BRITISH MEDICAL ASSOCIATION.

Balance Sheet as at December 31, 1954.

	£ s. d.	£ s. d.
FIXED LIABILITIES.		
Debentures—		
51—4% Series "A" at £10 each	510 0 0	
324—4·65% Series "B" at £50 each	16,200 0 0	
202—4·65% Series "C" at £10 each	2,030 0 0	
	18,740 0 0	
Less Amount Unpaid	54 0 0	
	18,686 0 0	
General Reserve Fund (used in the Branch Business)	1,250 0 0	
Australian Mutual Provident Society (Secured by Mortgage over Property, British Medical Association House)	20,000 0 0	
		39,936 0 0
CURRENT LIABILITIES.		
Sundry Creditors	1,607 12 8	
Deposit at Call	700 0 0	
Commercial Banking Company of Sydney, Limited—Branch and Premises Current Accounts Net	4,497 6 10	
		6,804 19 6
OTHER CREDIT BALANCES.		
Subscriptions Paid in Advance Suspense Account	112 6 1	
Provision for Taxation	3,004 13 0	
Provision for Painting Building	4,000 0 0	
Provision for Long Service Leave	1,550 0 0	
Superannuation Fund Reserve Account (as *per contra*)	1,937 19 3	
		10,605 3 4
Accumulated Funds—		
Balance as at December 31, 1953	101,691 11 10	
Add Surplus Year ended December 31, 1954—		
Branch £3,686 16 11		
Premises 1,103 3 1	4,790 0 0	
		106,481 11 10
		£163,827 14 8

	£ s. d.	£ s. d.
FIXED ASSETS.		
Land and Buildings, British Medical Association House—at cost *less* Depreciation on Building	131,138 10 11	
Library, at cost *less* Depreciation	7,787 9 4	
Office Furniture and Equipment at cost *less* Depreciation	2,028 13 1	
Debentures in Other Companies—		
Australasian Medical Publishing Company, Limited—Face Value	9,600 0 0	
Deposit on Debentures, Australasian Medical Publishing Company, Limited	165 0 1	
Commonwealth Treasury Bonds, Face Value	7,000 0 0	
		157,719 13 5
FLOATING ASSETS.		
Sundry Debtors, after making provision for Doubtful Debts, Sundry Tenants, Rent *et cetera*	3,890 4 9	
Cash on Hand	16 19 9	
		3,907 4 6
Other Debit Balances—		
Prepaid Insurances, Rates *et cetera*	262 17 6	
Superannuation Fund—Investment Account (as *per contra*)	1,937 19 3	
		2,200 16 9
		£163,827 14 8

Sydney,
February 15, 1955.

T. Y. NELSON, President.
GEORGE BELL, Honorary Treasurer.
G. D. ALEXANDER, Accountant.

We have examined the foregoing Balance Sheet with the Books of Account of the New South Wales Branch of the British Medical Association and having obtained all the information and explanations we have required, we are of the opinion that such Balance Sheet is properly drawn up so as to exhibit a true and correct view of the state of the Company's affairs according to the best of our information and the explanations given to us and as shown by the Books of the Company. In our opinion the Register of Members and other records which the Company is required to keep by the New South Wales Companies Act, 1936, or by its Articles have been properly kept.

Sydney.

F. W. DUMBRELL & Co.,
Chartered Accountants (Aust.).

Company Formation by Medical Practitioners.

During the year consideration was given by the Federal Council to the formation of companies by medical practitioners for the purpose of carrying on medical practice. The opinion was expressed by the Federal Council that such action was prejudicial to the doctor-patient relationship, and undesirable. In this the Federal Council had the full support of the Council of the New South Wales Branch. No objection is taken to the formation of companies for the purpose of acquiring property in which to carry on practice.

Group Practices: Use of Descriptive Titles.

Advice was received from the Federal Council to the effect that it was not opposed to the use of the term "clinic" in connexion with group practices, but was opposed to the title of newly formed groups being associated with the name of a suburb, town or district.

In this the Federal Council has the support of the Council of the New South Wales Branch.

Mass Immunization against Diphtheria.

Following representations made by Council, the Department of Health agreed to the remuneration payable to medical practitioners for services rendered in mass immunization campaigns against diphtheria being increased to £3 3s. for the first hour and £1 1s. for each subsequent hour or part thereof, subject to a maximum fee of £6 6s. for any one session.

World Medical Association.

The Council has established itself as a Supporting Committee of the World Medical Association, whose objects are, *inter alia*:

1. Promotion of closer ties among national medical associations and doctors.
2. Maintenance and protection of the honour and interests of the medical profession.
3. Presentation of world medical opinion to the World Health Organization (W.H.O.) and the United Nations Educational, Scientific and Cultural Organization (U.N.E.S.C.O.).

The World Medical Association affirms the views of the practising medical profession regardless of whether they agree or conflict with those held by governments.

Up to the present, the expenses of the World Medical Association have been largely provided by members of the American Medical Association forming themselves into a supporting committee. In order that Australia may do its share, supporting committees have been formed in each State.

By-Laws.

By-law 4 (annual subscription) was amended at an extraordinary general meeting of the Association held on December 9, 1954.

The amendment, which made no alteration to the rates of subscription, was rendered necessary by reason of the fact that the provision of the by-law for a reduced rate of subscription of three guineas in respect of a member admitted before the expiration of three years from the date of his registration as a legally qualified medical practitioner ceased to apply at December 31, 1953.

Committee for Placement of Resident Medical Officers.

The Committee for Placement of Resident Medical Officers, on which the Association has a representative, was again actively engaged in the allocation of resident medical officers to hospitals following the final degree examination which was held at the end of 1954. Since its inception the committee has been called upon to deal with the problem of finding sufficient vacancies in the hospitals for the large numbers who graduated.

With a reduction in this number at the end of 1955 to 173, the position was reversed, there being insufficient graduates for the number of vacancies. It was necessary to see that there was an equitable distribution of resident medical officers amongst the metropolitan and country hospitals, having regard to their requirements and to the fact that in the early years of the committee's activities it was indicated to hospitals that specially created new appointments, that their interests would be safeguarded in the future.

The lifting by proclamation of the suspension of the operation of Clause 17 (3) of the *Medical Practitioners' Act* now

NEW SOUTH WALES BRANCH OF THE BRITISH MEDICAL ASSOCIATION.

BRANCH ACCOUNT.

Income and Expenditure Account for the Year ended December 31, 1954.

	£ s. d.	£ s. d.
To Salaries	10,069 16 0	
„ Rent, Offices *et cetera*	1,200 0 0	
„ Printing and Stationery	1,393 18 3	
„ Stamps and Telegrams	798 12 0	
„ Telephones	303 11 3	
„ Travelling Expenses—General	286 11 5	
„ Code Address	3 8 0	
„ Insurance	40 3 8	
„ Exchange and Bank Charges	10 17 2	
„ Refreshments—Meetings	59 7 10	
„ Newspapers	68 6 4	
„ Sundry Petty Expenses	59 9 9	
„ Tea Money	120 6 0	
„ Federal Council	3,782 2 0	
„ Legal Expenses	48 7 0	
„ Repairs and Maintenance Equipment	165 17 9	
„ Pay Roll Tax	192 6 9	
„ Medical Benefits Fund—Staff	20 2 6	
„ Staff Superannuation Fund	583 3 1	
„ Incidental, Travelling and Entertaining Expenses	324 0 0	
„ Bank Interest	28 13 0	
„ Stamp Duty	34 4 10	
„ Expenses—Cricket Match	5 5 0	
„ Donation—Monograph Fund	250 0 0	
„ Fares and Cartage	29 9 5	
		19,877 19 0
„ Depreciation—		
Library	674 1 1	
Furniture and Equipment	165 17 4	
		839 18 5
„ Provision for Long Service Leave		400 0 0
„ Balance, being Surplus for year ended December 31, 1954, transferred to Accumulated Funds Account		3,686 16 11
		£24,804 14 4

	£ s. d.	£ s. d.
By Subscription Revenue		30,995 18 6
Less Proportion due to—		
British Medical Association	5,932 11 9	
THE MEDICAL JOURNAL OF AUSTRALIA	1,844 17 6	
		7,777 9 3
		23,218 9 3
„ Interest	533 7 7	
„ Rent Assembly Hall	541 16 0	
„ Broadcasting and Journalist Fees	321 16 6	
„ Accountancy Fees	100 0 0	
„ Refund Expenses Federal Council	89 5 0	
		1,586 5 1
		£24,804 14 4

renders it necessary for each graduate to act as a medical officer to a hospital or some other institution approved by the New South Wales Medical Board before he is entitled to practise his profession.

Department of Medical Sociology and Research.

Health education has been, as in previous years, the chief work of the department. Radio talks were given by the spokesman of the Association, and many articles on health and medical subjects, for Press use, were prepared and published.

A reference to the Association's work in popular education was contributed to a seminar, held at Canberra, on health education. This stated that the essential objective had been to assist in raising the standard of public health, through simple teaching of the general principles of scientific medicine, while emphasis was placed on the need of promoting understanding and cooperation in matters of health and the treatment of sickness, between the individual layman and his doctor. It was mentioned that with these aims broadcast talks of various kinds, numbering over a period of years many hundreds, had been given by the spokesman of the Association on health and medical subjects.

Golf Tournament.

The annual golf tournament for the British Medical Association Cup presented by Dr. H. C. Rutherford Darling was held on the golf course of the Australian Golf Club at Kensington on Tuesday, November 9, 1954. Dr. O. Robertson was the winner and Dr. J. F. Ward the runner-up. Trophies were presented at the Branch meeting on November 25, 1954.

The British Medical Agency of New South Wales, Limited.

The annual general meeting of the British Medical Agency of New South Wales, Limited, was held on October 5, 1954. The report of the directors was presented by the Chairman, Dr. George Bell.

There was an improvement in the financial position of the Company, the profit for the year showing an increase of 50% on that of the previous year.

Once again the directors look to members of the profession to give their continued support to their own agency.

Medical Finance Limited.

The annual general meeting of Medical Finance Limited was held on October 5, 1954. In presenting the annual report of the directors for the year ended June 30, 1954, the Chairman, Dr. George Bell, indicated that a small profit had been made for the year. He pointed out as in previous years that, whilst more attractive interest rates for borrowers are offered elsewhere, the demand for the Company's funds must continue on a limited basis.

Premises Revenue Account.

The Premises Revenue Account discloses a net surplus of £1104, as against a net surplus of £1873 for the year ended December 31, 1953, thus showing a decrease of £769 in the net revenue earned. This decrease is accounted for by a net increase in income of £896 and a net increase in expenditure of £1665, as set out in detail in the accompanying comparative statement.

A comparison of percentages of expenditure to rent revenue with those at December 31, 1953, is as follows:

	1953.	1954.
Percentages of expenses to revenue ..	93·3%	96·5%
Percentages of surplus to revenue ..	6·7%	3·5%
	100·0%	100·0%

The percentage of rent revenue, expenses and depreciation and the percentage of net surplus for the year to the capital value of the land and building (British Medical Association House) as shown by the books at December 31, 1954, namely, £131,139, with the previous year's percentages in parentheses, are as follows:

Rent revenue (including amount charged for British Medical Association Branch offices *et cetera*)		21·9%	(20·9%)
Sundry expenses, interest and provision for painting of building	18·9%		(17·3%)
Depreciation of building	2·1%	21·0%	(2·1%)
		0·9%	(1·5%)

Financial Statement.

The Council has pleasure in presenting to members the balance sheet and accounts in respect of the financial year which terminated on December 31, 1954.

The net surplus of revenue over expenditure for the year amounted to £4790 after making provision for all known expenditure.

The sum of £3658 3s. 8d. has been written off for depreciation of the building (British Medical Association House), plant, office furniture and equipment and the library.

The sum of £800 has been provided out of the current year's revenue to create a reserve for painting of the exterior of the building and £425 as a provision for long service leave. These amounts for the time being are used in the business of the Association.

T. Y. NELSON,
President.

The balance sheet of the Branch and the income and expenditure account of the Branch and of the premises were received and adopted on the motion of Dr. George Bell, seconded by Dr. W. F. Simmons.

ELECTION OF OFFICE-BEARERS.

Dr. T. Y. Nelson announced that the following had been elected representatives of the Council for the ensuing year: Dr. M. S. Alexander, Dr. George Bell, Sir Charles Blackburn, Dr. B. T. Edye, Dr. H. R. R. Grieve, Dr. G. C. Halliday, Dr. G. L. Howe, Dr. A. S. Johnson, Dr. R. H. Macdonald, Dr. A. W. Morrow, Dr. A. J. Murray, Dr. K. C. T. Rawle, Dr. W. F. Simmons, Dr. E. S. Stuckey, Dr. E. F. Thomson, Dr. H. I. Turnbull.

Elected as Representing the Public (Government) Medical Services.—Dr. E. T. Hilliard.

Elected as Representing Country Local Associations.—Dr. B. A. Cook. (This was the only nomination received.)

Elected as Representing Metropolitan Local Associations.—Dr. K. S. Jones, Dr. C. R. M. Laverty.

No representative of the women members had been nominated.

Messrs. F. W. Duesbury and Company were elected auditors for the ensuing year.

ELECTION OF REPRESENTATIVES OF THE BRANCH AT THE ANNUAL REPRESENTATIVE MEETING AND AT THE ANNUAL MEETING OF THE BRITISH MEDICAL ASSOCIATION, 1955, AT TORONTO, CANADA.

On the motion of Dr. W. F. Simmons, seconded by Dr. E. F. Thomson, the election of representatives of the Branch to attend the Annual Representative Meeting and the annual meeting of the British Medical Association, 1955, to be held at Toronto, Canada, was left in the hands of the Council.

INCOMING PRESIDENT'S ADDRESS.

Dr. H. H. Willis delivered his incoming President's address (see page 897). A vote of thanks to Dr. Willis for his address was carried on the motion of Dr. Angus Murray, seconded by Dr. A. W. Morrow.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

STRABISMUS OR SQUINT.

[From the *Hobart Town Advertiser*, March 11, 1842.][1]

AN operation for this very disagreeable mal-direction of the visual organ has been performed in this town for the first time with perfect success. Dr. Brock was the operator, in the presence of Dr. Clark and several medical gentlemen. The party Charles Monk aged 36 had laboured under the

[1] From the original in the Mitchell Library, Sydney.

defect from childhood, occasioned by the smallpox. The eye was considerably reversed, but immediately the operation (which occupied not more than 3 minutes) was effected, it recovered its natural position: the effusion of blood was very slight; and the pain but trifling. The French physician who discovered this operation (which consists in dividing the distorted muscle) has been raised to the nobility by the King of the French.

Congress Notes.

AUSTRALASIAN MEDICAL CONGRESS (BRITISH MEDICAL ASSOCIATION).

THE following notes relate to the Australasian Medical Congress (British Medical Association), Ninth Session, to be held at the University of Sydney from August 20 to 27, 1955.

Scientific Exhibition.

The scientific exhibition, which will be housed in the Drawing Room, Department of Electrical Engineering, University of Sydney, will include the following demonstrations *inter alia*.

1. Fairfax Institute of Pathology, Royal Prince Alfred Hospital, Sydney: Benign tumours of the lung; hepatic duct tumours.

2. Hallstrom Institute of Cardiology, Royal Prince Alfred Hospital, Sydney: Chronic valvular disease of the heart.

3. Kanematsu Institute, Sydney Hospital, Sydney: Salivary gland tumours; lipid transport and its possible relation to atherosclerosis.

4. Department of Radiology, Royal Prince Alfred Hospital, Sydney: Practical demonstration of tomography.

5. Kolling Institute, Royal North Shore Hospital, Sydney: The pathogenic fungi.

6. Prince Henry Hospital, Sydney: Laboratory diagnosis of virus diseases (psittacosis, poliomyelitis, *herpes zoster*).

7. Department of Pathology, St. George Hospital, Sydney: Some interesting pathological specimens.

8. Department of Medicine, Medical School, University of Sydney: Diseases of the œsophagus.

9. Department of Surgery, Medical School, University of Sydney: Hydatid disease.

10. Department of Obstetrics, Medical School, University of Sydney: Exhibit.

11. Department of Pathology, Medical School, University of Sydney: The pneumoconioses by large lung section technique.

12. Department of Dermatology, Medical School, University of Sydney: Demonstration of skin diseases.

13. Saint Vincent's Hospital, Melbourne: Hæmodynamics of anæmia.

14. The Medical Services of the Navy, Army and Air Force: Aspects of naval, army and aviation medicine.

15. Red Cross Blood Transfusion Service, New South Wales: Aspects of blood transfusion and blood group ethnology.

16. Pharmaceutical Society, New South Wales: A display of the official preparations of the British Pharmacopœia and the British Pharmaceutical Codex.

Notice.

VICTORIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION.

Section of Industrial Medicine.

THE next meeting of the Section of Industrial Medicine of the Victorian Branch of the British Medical Association will be an evening plant tour embracing inspection of the

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED MAY 28, 1955.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	2	1(1)	2(2)	..	..	..	..	..	5
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	1	1(1)	..	..	..	..	7	..	9
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	1	..	..	..	..	..	..	..	1
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	2(2)	13(12)	1	..	..	..	..	..	16
Diphtheria	4(3)	3(3)	3(3)	..	43(28)	..	..	..	53
Dysentery (Bacillary)	..	1(1)	1(1)	..	2(2)	1	..	..	5
Encephalitis	..	..	..	..	..	..	..	..	..
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	44(10)	57(22)	..	1	9(5)	..	1	..	112
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	1(1)	..	..	..	..	1	..	2
Leptospirosis	..	..	5(1)	..	..	..	..	..	5
Malaria	..	1(1)	1(1)	..	3(3)	..	8	..	13
Meningococcal Infection	1(1)	1	..	..	..	1	..	..	3
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	1(1)	..	..	..	..	..	..	..	1
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	..	4(2)	1(1)	2(2)	..	..	..	..	7
Puerperal Fever	..	..	1(1)	..	..	..	..	..	1
Rubella	..	8(4)	4	..	3(3)	..	..	..	15
Salmonella Infection	..	..	..	..	2(2)	..	1	..	3
Scarlet Fever	14(10)	14(10)	9(1)	4(4)	1(1)	..	..	..	42
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	1	..	..	2	..	..	..	3
Trachoma	..	..	..	..	5(5)	..	..	..	5
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	29(21)	10(7)	25(7)	3(2)	10(9)	4(1)	..	..	81
Typhoid Fever	..	1	..	..	..	..	1	..	2
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	1(1)	..	..	..	1
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

foundry, plating shop and plastic moulding department operations at Die Casters, Limited, corner of Gipps and Islington Streets, Collingwood. The Industrial Hygiene Department of the State Health Department will demonstrate the hazards of plating operations and methods of resuscitation in cyanide poisoning cases. All interested members both of the Section and of the Branch are invited to assemble at the main entrance at 7.45 p.m. on Tuesday, June 21, 1955. Supper will be served.

Honours.

BIRTHDAY HONOURS.

THE following are included among the Birthday Honours awarded by Her Majesty Queen Elizabeth II.

Dr. Albert Ernest Coates, of Melbourne, Dr. D'Arcy Rivers Warren Cowan, of Adelaide, and Professor Harold Robert Dew, of Sydney, have been created Knights Bachelor.

Dr. Benjamin Keith Rank, of Melbourne, and Dr. Allan Robert Stanley Vickers, of Charleville, Queensland, have been created Companions of the Most Distinguished Order of Saint Michael and Saint George.

Dr. John Lewers Grove, of Launceston, Dr. William Caldwell McLelland, of Melbourne, and Dr. Frederick Grantley Morgan, of Melbourne, have been created Commanders of the Most Excellent Order of the British Empire.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Annual Subscription Course.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that Professor R. Hare, M.D., Professor of Bacteriology in the University of London and Honorary Consulting Bacteriologist, St. Thomas's Hospital Medical School, London, will give the following lectures:

Monday, June 27, at 8.15 p.m., "Hospitals as Reservoirs of Infection", in the Stawell Hall, 145 Macquarie Street, Sydney.

Wednesday, June 29, at 8 p.m., "The Anaerobic Cocci", in the Robert H. Todd Assembly Hall, 135 Macquarie Street, Sydney, in conjunction with the Australian Association of Pathologists and the Section of Pathology.

Friday, July 1, at 1.15 p.m., "The Conquest of Puerperal Infection", in the Scot Skirving Lecture Theatre, Royal Prince Alfred Hospital, Camperdown.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Malecki, Joseph, registered in accordance with the provisions of Section 17 (1) (c) of the *Medical Practitioners Act*, 1938-1953, 6 Harris Street, Fairfield, New South Wales.

Vince, John, registered in accordance with the provisions of Section 17 (1) (c) of the *Medical Practitioners Act*, 1938-1953, 29A Penkivil Street, Bondi, New South Wales.

The undermentioned have applied for election as members of the South Australian Branch of the British Medical Association:

Wilson, Pauline Ina, qualified 1954, 7 Pine Street, Woodville Gardens, South Australia.

Edgar, Oscar Patrick, qualified 1955, 22 Sturt Street, Saint Leonards, South Australia.

Shakes, David James, qualified 1955, 15 Cedar Avenue, Croydon, South Australia.

Lam, Lambert Teck Choon, qualified 1955, 35 South Terrace, Adelaide.

Tassie, Gemmel Wilson, qualified 1955, 6 Sinclair Court, 451 Anzac Highway, Camden, South Australia.

Horvat, Victor, qualified 1955, 81 Kensington Road, Norwood, South Australia.

The undermentioned have been elected as members of the South Australian Branch of the British Medical Association: Hyde, James O'Halloran, qualified 1953; Lawrence, James Roland, qualified 1953; Holle, Edward Murray, qualified 1952.

Diary for the Month.

JUNE 21.—New South Wales Branch, B.M.A.: Medical Politics Committee.
JUNE 22.—Victorian Branch, B.M.A.: Branch Council.
JUNE 23.—New South Wales Branch, B.M.A.: Clinical Meeting.
JUNE 23.—South Australian Branch, B.M.A.: Scientific Meeting.
JUNE 24.—Queensland Branch, B.M.A.: Council Meeting.
JUNE 28.—New South Wales Branch, B.M.A.: Ethics Committee.
JUNE 29.—South Australian Branch, B.M.A.: Annual Meeting.
JUNE 30.—New South Wales Branch, B.M.A.: Branch Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all contract practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

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